Final Draft

INFORMAL REVIEW

Diarrheal and Respiratory Disease Research and Coordination Project

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Office of Health and Nutrition

U S Agency for International Development

by

Abraham Horowitz, M D , M P H
David Sencer, M D , M P H
Susan Zimicki, M S P H

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Prepared by
Statistica, Inc
1800 N Kent Street
Room 1050
Rossslyn, VA 22209

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Acronyms and Abbreviations

ADDR	Applied Diarrheal Disease Research
ARI	Acute Respiratory Infection
BASICS	Basic Support for Institutionalizing Child Survival
CA	Cooperative Agreement
CDD	Programme for the Control of Diarrheal Diseases
CDR	Division of Diarrheal and Acute Respiratory Disease Control
CS	Child Survival
CSAP	Child Survival Action Program
CVI	Children's Vaccine Initiative
DDRC	Diarrheal Disease Research and Coordination
DRDRC	Diarrheal and Respiratory Disease Research and Coordination
EHP	Environmental Health Project
EPI	Expanded Programme on Immunization
GNP	Gross National Product
HIID	Harvard Institute for International Development
ICDDR,B	International Centre for Diarrhoeal Disease Research, Bangladesh
IIP	Institute for International Programs (JHU)
IDRC	International Development Research Centre (Canada)
IMCI	Integrated Management of Childhood Illness
JHU	Johns Hopkins University
JHU/QAP	Johns Hopkins University Quality Assurance Project
LAC	Latin America and Caribbean Bureau
LDC	Lesser Developing Countries
NIH	National Institutes of Health (U S)
OMNI	Opportunities for Micronutrient Interventions
ORS	Oral Rehydration Solution
ORT	Oral Rehydration Therapy
PASA	Participating Agency Service Agreement
PATH	Program for Appropriate Technology Health
UNDP	United Nations Development Program
USAID	U S Agency for International Development
UNICEF	United Nations Children's Fund
WHO/CDR	World Health Organization/Control of Diarrheal and Respiratory Diseases
WHO/CTD	World Health Organization/Control of Tropical Diseases
WHO/GPV	World Health Organization/Global Programme on Vaccines
WHO/TDR	World Health Organization/Tropical Disease Research
WHO	World Health Organization

Table of Contents

C

Executive Summary

A mid-project review of the Diarrhea and Respiratory Disease Research and Coordination (DRDRC) Project was undertaken in the fall of 1994 The purpose of the review was to assess progress and performance and to identify research gaps and research topics where support might be made more limited Three external reviewers assisted in the process Dr Abraham Horowitz, former Minister of Health in Chile and Director of PAHO, currently Director Emeritus of PAHO, Dr David Sencer, former Director of CDC, currently a private consultant, Ms Susan Zimicki, former Research Director, Center for International Health and Development, Annenberg School of Communications, University of Pennsylvania, currently a private social science/communications consultant The review was informed by input from USAID staff in missions, regional bureaus, the Bureau for Policy and Program Coordination, the Office of Health and Nutrition, cooperating agencies, and by the review of documents including annual reports and subproject-specific evaluations

The DRDRC Project is performing extraordinarily well, having already exceeded many of its end-of-project targets The achievements of the subprojects are significant and impressive The DRDRC Project implements good, cost effective, applied research Research studies have been mainly short term (less than 2-3 years), multidisciplinary, and influential with respect to policy and programs worldwide Redundancy has been avoided through active coordination of activities Overheads, indirect costs, and support costs outside developing countries are low An estimated 90% of research grant funds go to developing country institutions and investigators, with direct benefits for developing countries

Multidisciplinary research and research capacity building constitute important aspects of the project Behavioral research is integrated with biomedical research Furthermore, social science represents approximately 19% of all the research, important interventions to influence behavior change have been identified, tested and incorporated into training strategies and education of both providers (pharmacists and physicians) and caretakers (mainly mothers) Research capacity building illustrates just what a development agency should do--generate important research results, translate these results into policy and programs, and create capacity for self sufficiency in developing countries The achievements of ADDR and ICDDR/B in this area of capacity building are especially remarkable and critical for the development of self reliance Future success is threatened, however, by steadily declining USAID funding for health research

The excellent performance of the project has been due to the quality of the institutions managing the research (ICDDR,B, WHO/CDR and ADDR), the active involvement and competence of their directors, and the effective leadership of the USAID project manager, Dr Caryn Miller, who has been the intellectual force behind the project Since 1991 Dr Miller has guided and coordinated the involvement of the research institutions in this project and has paid particular attention to ensuring the complementarity of the DRDRC-funded research, thus enhancing the project's potential policy and programmatic impact With this approach she has shown how USAID can contribute effectively to the analysis and solution of important health problems in the developing world--problems with a heavy burden of disease, death, and disability The project benefits from the collaborative and open relationship between USAID and its implementing organizations--one which fosters mutual respect reflecting a true partnership

The project has shown flexibility as well as vision in responding to evolving health situations in developing countries Each of the cooperating agencies as well as USAID, use a variety of mechanisms for resetting research priorities Over time, allocation of resources has shifted from diarrheal disease to ARI and from case management to prevention (reflecting the growth in knowledge as interventions are successfully identified and tested and the concomitant evolution of the information needs of policymakers) However, since diarrhea actually represents a constellation of causative agents, resources in the future will be required for dealing with the treatment of invasive and persistent diarrheas and prevention, especially vaccines The project, with WHO/CDR taking the lead, has been bold in developing a more integrated approach to treating sick children Continuing progress in this area, including behavioral/social research on issues such as development of more effective training of practitioners and promotion of appropriate careseeking, is a priority Other research areas identified as priorities included a) development of simple, cost-effective surveillance methods (for example, to monitor microbial resistance or to document the specific impact of interventions on morbidity and mortality), b) further development and/or assessment of selected interventions (such as reduction of indoor air pollution, improvement of feeding during diarrhea, micronutrient supplementation, hygiene, vaccines), and c) behavioral and management research on factors influencing quality of care at public and private health facilities In addition, the interest of the institutions in developing meaningful indicators for measuring research progress, research capacity building and in dissemination of results was encouraged

Given its success to date, the DRDRC project appears to be uniquely qualified to address these issues

I Purpose of Review (Caryn Miller)

The purpose of this informal review of the Diarrheal and Respiratory Disease Research and Coordination (DRDRC) Project is two-fold The first purpose is to review the project's performance to date and its progress in achieving targets set in 1991 The second purpose is to identify gaps in research and areas within the project where research support can be decreased The review will be informed by input from USAID staff in missions, regional bureaus, the Bureau for Policy and Program Coordination, and the Office of Health and Nutrition as well as staff of USAID's cooperating agencies Reviewers were sent annual reports and subproject-specific evaluations as background materials

II Current Status of the DRDRC Project

A Evolution of the DRDRC Project (Caryn Miller)

The purpose of the DRDRC Project is to improve the health status of developing country populations through reductions in childhood mortality and morbidity due to diarrheal and respiratory diseases The project fills the critical gap between basic research and field implementation through applied research aimed at targeted goals The project focuses on three key areas 1) supporting high quality, multi-disciplinary research in priority areas of prevention and improved case management, 2) strengthening developing country institutions and researchers so that they will have the capability to manage and sustain research activities in essential national health areas, and 3) promoting coordination and collaboration between and among researchers, care providers, decision-makers, and program managers at all levels in order to make research efforts more efficient and cost effective

Prior to 1991, the USAID Office of Health funded research in child survival through separate projects implemented by the Harvard Institute for International Development (ADDR Project), the WHO Programme for the Control of Diarrhoeal Diseases (grant to WHO/CDD), the International Centre for Diarrhoeal Disease Research, Bangladesh (ICDDR,B), a cooperative agreement with Johns Hopkins under the Child Survival Action Program (JHU/CSAP), and a vaccine PASA with the U S Department of Health and Human Services In 1991 USAID initiated the DRDRC Project's predecessor, the Diarrheal Disease Research and Coordination (DDRC) Project The DDRC Project focused on global and country level diarrheal disease research, and the implementors were the ICDDR,B and WHO/CDD In 1992, the DDRC Project was amended as the DRDRC Project in order to broaden its activities to include research related to ARI, TB, measles, and malaria and to incorporate research implemented by the ADDR Project and the WHO Programme for the Control of Acute Respiratory Infections (WHO/ARI) Upon completion of the vaccine PASA, vaccine research was accomplished through DRDRC, and a new project, the Children's Vaccine Initiative (CVI) Project, was put in place to focus on ARI vaccines It is anticipated that follow-on activities of the JHU agreement will be placed under the DRDRC umbrella

Despite the larger mandate, the project's only additional funding was for ARI ($750,000/year) Two other subcomponents of the amended project were never implemented except in a very limited way because no additional funds were allocated These subcomponents were a PASA with CDC for accelerating the development of methodologies for monitoring microbial drug resistance and agreements to implement coordination and dissemination activities

In 1995, it is anticipated that the project will be extended five years to the year 2001 If funds are available, activities currently supported by the JHU-1 subcomponent of the Child Survival Action Program will be incorporated into the DRDRC Project The PASA with CDC for monitoring microbial drug resistance is also planned and a small grant to the Commission on Health Research for Development (COHRED) for development of national health research agendas is under consideration

B Analysis of Health Research Supported by USAID (Caryn Miller)

USAID funding for population, health, and nutrition was 44% of total development assistance in FY94 USAID funding for all health activities amounted to $614 million in FY94, research[1] constituted 6 8% ($41 8 million) of that amount, as shown in Figure 1 (By comparison, the FY94 budget for the DRDRC Project was $5 8 million) Figure 2 compares research funding for different types of activities in FY93 Nearly one third of research dollars were spent in the area of HIV/AIDS (32%) The remaining types of activities and their relative allocations were child survival (22%), malaria/vector-borne diseases (21%), health systems development (17%), women's health and nutrition (4%), and other miscellaneous activities (4%) Figure 3 shows that USAID's Global Bureau implemented 80% of health research in FY94 Figure 4 shows that funding for health research over the period 1985-1994 amounted to $ 646 million, or 14% of USAID's total obligations for health during that time Figure 5 shows that funding for health research grew steadily through FY93 but has dropped precipitously in FY94 FY 95 estimates project an additional 75% decrease

C Analysis of the DRDRC Project Trends and Progress in Reaching End of Project Targets (Kevin Callahan)

USAID obligations for the DRDRC Project have averaged about $6,000,000 each year since the project's inception (Figure 6) The funding for research grants and contracts has risen steadily during that period (Figure 7) *All of the following data refers to*

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[1] *Unless otherwise noted research discussed in this report conforms to USAID s definition of research which is*

The systematic investigation of a well-defined problem USAID supports research that is intended to produce knowledge that will offer solutions to specific development challenges This includes the spectrum of research that is required to foster marketable technology The research process incorporates a well-defined hypothesis a defined methodology for the gathering of information analysis of data, and for interpretation of the data to formulate conclusions This definition includes research experimentation and product development in all fields

This definition excludes routine product testing quality control geographic mapping collection of general purpose statistics experimental production and routine monitoring and evaluation of an operational program Research for the sole purpose of training scientific and technical personnel is not included.

funding for research grants and contracts only (ie no information is provided regarding funding for administration and technical support)

Geographical distribution. In FY93, 52% of overall funding for research grants and contracts went to the Asia and Near East region (reflecting in part the relatively large allocation for the ICDDR,B), and 28% to Latin America and the Caribbean, 18% percent to Africa, and 2% to Europe and the Newly Independent States of the former Soviet Union Besides Bangladesh, other countries receiving relatively large amounts of grant and contract support in FY93 were Peru, Guatemala, Nigeria, Ecuador, India, and Venezuela (Figures 8,9, and 10)

Disease distribution Fifty eight percent of overall funding for research grants and contracts in FY 91-93 supported research in diarrheal diseases, while ARI research captured 24% of funding Other disease categories were malnutrition related to diarrhea (13%), malnutrition related to ARI (1%), other malnutrition (3%), measles (<1%), and malaria (<1%) (Figure 11) Research in diarrheal diseases and malnutrition related to diarrhea has declined over that period, while research in ARI has increased (Figures 12-14)

Distribution with respect to type of research Laboratory-based applied biomedical research constituted 12% of funding, while clinic- and field-based evaluations of interventions (eg vaccine or algorithm trials) constituted 20% of funding and epidemiological research (eg baseline or risk factor studies) constituted 40% The other broad types of research and their relative funding levels were operations research[2], 5%, health systems and policy reform research, 4%, and social science and economic research (eg behavioral studies, cost-effectiveness studies), 19% (Figure 15) (Note that operations research for child survival interventions is funded largely through the cooperative agreement with Johns Hopkins University, while health systems and policy reform research is supported through several other projects within the Office of Health and Nutrition)

Distribution with respect to case management versus prevention Funding for research in prevention has consistently exceeded funding for research in case management In FY92, the amount spent for prevention research was nearly twice that for case management research In FY93, while the amount for prevention rose again, the amount for case management rose higher still (Figure 16) The rise over the FY91-FY93 period can largely be attributed to dramatic increases in prevention research implemented by WHO/CDD and ADDR, although ICDDR,B has consistently devoted more funds for prevention than for case management (Figure 17) Over the entire period, the amount spent for prevention research was 60% of the total (Figure 18)

Distribution with respect to categories of prevention The major categories of prevention research and their respective allocations for research grants and contracts in 1993 are nutrition (23%), vaccines (43%), breastfeeding (8%), hygiene (10%), indoor air pollution (7%), and other (8%) (Figure 19)

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[2] Operations research Using the scientific method to enable efficient and effective application of existing technologies and programs

Status of key indicators for measuring project progress. Midway through the project's lifetime, most of the end-of-project targets have already been achieved For example, targets for the number of completed research studies and the number of funded investigator have been exceeded The current number of individual investigators serving as first authors in peer-reviewed journals and the current number of investigators receiving key publications are close to target levels (Figure 20) In addition, the attached list of ICDDR/B achievements and institutional collaborations, together with the Centre's development of a strategic plan, indicate clearly that the ICDDR/B is accomplishing the targets given in the project paper

D Major Achievements of the DRDRC Project (Caryn Miller)

The major achievements of the project, as compiled by the project's three implementors, are listed in Appendix B The reviewers noted that research supported by the DRDRC Project addresses each of the perceived drawbacks of research, the research studies tended to be short, frequently produced results that are incorporated into policies and programs, and avoided redundancy The reviewers attributed part of the project's impressive list of achievements to the complementarity of the subprojects, as well as to the high competence of the subproject directors, and the effective leadership at USAID One reviewer said, "Although difficult to measure, one is inclined to believe that the applied outcomes of a number of studies, must have contributed to the decline in mortality rates due to CDD and ARI in many countries of the world "

Dissemination of research results has been accomplished through a variety of mechanisms, including peer-reviewed publications, workshops, presentations to national policy makers, and presentations at national and international meetings

Highlights of the research achievements include

1 The overall success rate of an algorithm for the management of persistent diarrhea in hospitalized children was found to be close to 90% WHO will include the algorithm as part of the standard recommended treatment guidelines for persistent diarrhea in children Significant savings will be realized from using this algorithm because it involves lower food costs, reduced medication use, and reduced duration of hospital stays

2 Vitamin A supplementation was associated with as much as a 23% reduction in the incidence and duration of severe diarrhea In a related development, supplementation of mothers with high doses of Vit A soon after delivery was shown to result in significant reduction of mortality in breast-feeding infants under 6 months of age

3 A community based trial of cotrimoxazole in children with suspected pneumonia in the Northern Areas of Pakistan showed that this drug of choice was effective in 91% of pneumonia cases, despite laboratory data showing high levels of bacterial resistance At a savings of $1 85/episode, with an estimated 18 million treatable episodes of pneumonia per year in children, the Pakistan

ARI Programme will save millions of dollars and achieve higher levels of patient compliance

4 Vibrio cholerae 0139 was identified as a new pathogen causing a disease identical to cholera caused by 01 Rapid identification of this organism helped to alert the international community to the emergence of a new threat of disease Clinical and epidemiological characterization provided information on management and control to affected areas and has contributed to the development of the new generation of cholera vaccines that will be protective against both 01 and 0139 In a related development, Vibrio cholerae 01 were shown to be present in the mucilaginous sheath of a blue green algae present in natural aquatic environment This finding provides new directions for global control of the disease

5 A program for supporting researchers adapted to the local academic and political environment, combining workshops, consultant assistance, and learning by experience, can overcome many of the structural constraints to building capacity for responding to rapidly changing health problems

6 The ICDDR/B has developed methodologies and established procedures for rapid and effective responses to diarrhea epidemics This capability was shown to be critical, unique and effective during the recent cholera and shigella epidemics amongst Rwandan refugees in Goma, Zaire, and was in stark contrast to ineffective, often harmful and ill-formed response of several other NGO's operating at the same time As a result, USAID's Office of U S Foreign Disaster Assistance has proposed that the ICDDR/B design off-site and on-site training courses to increase quality response

7 A series of reviews of risk factors for childhood pneumonia and potential impact on pneumonia morbidity and mortality of interventions to reduce these risk factors suggest that high priority be given to studies on H influenzae and conjugated pneumococcal vaccines and indoor air pollution These reviews have proved very useful in guiding research, development and implementation activities

8 Research in Pakistan showing the dangerous side effects of anti-diarrheal drugs in children prompted the national government to prohibit or tightly regulate the use of these drugs Sixteen other developing countries have followed suit

9 Educational and managerial interventions in a Mexican Social Security (IMSS) clinic significantly reduced the proportion of children who received antibiotics and antidiarrheals, and increased ORS use These changes have lasted more than 18 months after the intervention ended Medication compliance improved among patients in the intervention group even though this was not an explicit objective of the intervention A second study undertaken by the IMSS extended the methods to 17 clinics from both the IMSS and the Mexican Ministry of Health, and looked both at diarrheal diseases and ARI

Results from this randomized controlled trial of clinics were also successful, with medication costs decreasing by 36% and medication waste due to noncompliance and overprescribing decreasing by 51% The IMSS is now implementing a new diarrheal disease treatment program in 12 Mexican states

III Special Topics

A Research Capacity Building (Jim Trostle)

The ADDR Project convened a meeting (September 29-30, 1994) for the purpose of developing indicators for research capacity building Participants from HIID WHO/TDR, WHO/HRP, IDRC, USAID, and other institutions agreed that useful evaluation tools could be developed The group clarified definitions and methodologies and agreed to test certain indicators through their current projects ADDR plans to synthesize ideas from the participants on three levels individual, institutional, and network based It will then convene a larger meeting of donors and developing country representatives to further refine the indicators and after that, host an international, multi-sectoral conference

B The Chilean Experience (Abraham Horwitz)

Chile has achieved a dramatic decline in infant and child mortality independent of socio-economic level This achievement is principally the result of long-term political commitment to health and education for all (regardless of the political party in power), an emphasis on adequate nutrition and health care for mothers and infants, and improved sanitation Crucial to its success was the decision to treat children for malnutrition outside of traditional health care facilities An autonomous national health service also factored into the success Chile's achievement challenges the conventional wisdom that a developing country cannot afford expenditures for health care and education

C The Bangladesh Experience (Demissie Habte)

The infant mortality rate in Bangladesh has declined from 140 per thousand live births in 1975 to 91 per thousand live births in 1992 During that time period, economic growth (as measured by GNP) has not improved, nor have there been overall improvements in education levels, nutritional status, women's status, or general health services The percentage of women using appropriate breastfeeding practices has actually fallen The decline in the infant mortality rate can be attributed in part to very high rates of infant vaccination, recent studies suggest that almost 25% of the improvements in child survival are the result of decreased cases of the vaccine-preventable childhood diseases The dramatic decrease in the total fertility rate and the increase in the contraceptive prevalence rate have also been credited with improving maternal and child survival Other factors cited included a decline in deaths due to ARI as a result of appropriate case management, widespread Vitamin A distribution, and high levels of access to tube well water (although access to adequate sanitation remains low) The Bangladesh experience has shown that family planning and selected child survival interventions can produce dramatic declines in the infant mortality rate

independent of infrastructural and economic improvements Questions remain about the sustainability of the gains, however, given the lack of concomitant economic and social development Furthermore, little is known about the cause-specific mortality changes and impact on mortality of selected interventions

IV Identification of Research Gaps and Areas of Research Where Support Might be Limited or Reduced

A. **Development of Surveillance Methodologies for:**

1. Monitoring antimicrobial resistance (shigella, malaria, pneumonia, TB). It was recognized that monitoring of microbial resistance needs collaboration with others WHO/CDR has taken a lead role DRDRC should take a lead role in the development of a methodology for monitoring resistance to drugs used for pneumonia, as well as the training and technical assistance for monitoring resistance to shigella and the development of optimal drug regimens for shigella For developing country institutions where this capacity is being developed, consideration to strengthening laboratory capacity for TB and malaria should also be given National surveillance requires good labs and trained personnel and is expensive Sentinel surveillance and regional centers with laboratory capabilities should be considered Mission staff urged the use of existing networks, such as INCLEN Monitoring based on clinical failures rather than laboratory resistance is an alternative or complementary approach worth investigating Research issues will be further discussed at a consultancy convened by WHO/CDR in Geneva in January 1995 In addition, correct prescribing practices will slow the development of resistance Therefore, there is a need to focus on private practitioners (motives and incentives) and on legal approaches to changing and enforcing regulations

2 Anticipating and detecting emergence and re-emergence of infectious diseases, other new health threats, and epidemics such as cholera, malaria, and TB. Important methodologies include a) development of simple diagnostics that can be used to monitor the environment (e g cholera), b) identification of the conditions that bring about emergence/re-emergence, and c) development of methods for monitoring drug resistance and development of strategies to impede drug resistance (see above) DRDRC should focus on diseases within its mandate (ie diarrheal and respiratory disease)

3. Evaluating the efficacy of potential interventions such as pneumonia vaccines (e g correlates of immunity) **and monitoring the impact of interventions when applied in demonstration studies or programs.**

4. Documenting cause-specific mortality (e g verbal autopsies) and documenting impact of interventions on mortality

Disease priorities in each of the areas above would be pneumonia, shigella, and cholera Work in malaria should be coordinated with WHO/TDR and EHP and be limited to laboratory capacity strengthening in institutions where DRDRC has been involved LAC Bureau recommended that measles diagnostics be included, but the

external consultants stated this should not be a DRDRC priority Work in pneumonia and cholera should be coordinated with WHO/GPV and PATH DRDRC priorities for no 4 would be broader to include measles and malaria as well as persistent diarrhea DRDRC would not take a lead role in implementing proven methodologies in country programs Mission responses indicated a lead role for DRDRC in these areas with potential bilateral investment in strengthening surveillance

5. Documenting impact of interventions on morbidity. Long term strategic research is needed to lay the groundwork for monitoring morbidity and to look at the impact on morbidity of preventive strategies such as vaccines, improved hygiene and sanitation, behavior change, etc This research will complement EPI coverage surveys, the latter collect information about coverage (and from that estimate the impact on disease) while the former assesses the actual impact (which could exceed or fall below estimates)

B. **Diarrheal disease vaccine research focusing on epidemiological studies and field evaluation** This area is important for diarrhea requiring antibiotics (e g shigella) because of increasing drug resistance and for diarrheas causing epidemics (e g cholera) No other USAID projects are working in this area, and it was considered by mission staff to be important, but one that should be supported by the Global Bureau rather than through bilateral funding

C **ARI prevention** Potential cost-effective and feasible interventions for ARI prevention have been identified in an extensive review by the London School of Hygiene

1. Vaccines. The Haemophilus influenzae b (Hib) vaccine is currently being evaluated for its efficacy against pneumonia and meningitis in The Gambia through DRDRC (WHO/CDR), UNICEF, and UNDP At least one pneumococcal vaccine trial will begin this year with funding probably from WHO/CDR, Praxis Lederle, NIH, and the CVI Project (pending availability of funds) It is anticipated that future funding for ARI vaccine evaluation will come from USAID, either directly from the CVI Project or indirectly through WHO/CDR

2. Vitamin A. Several trials are underway to look at safety, improvement of vitamin A status (in children under 6 months through postpartum supplementation of mothers and in children through EPI-linked supplementation), and short-term impact on morbidity, including ARI Additional funds will be needed to study long-term impact on morbidity and mortality resulting from ARIs

3 Reduction of indoor air pollution The potential use of locally manufactured cook stoves to reduce indoor air pollution is being evaluated in Guatemala for its impact on pneumonia WHO/CDR and IDRC have funded the baseline/development activities Intervention trials in Guatemala and elsewhere will require additional resources

4. Chilling Skepticism surrounds this risk factor However, a review of the literature confirms it as a risk factor in animals For the neonate, UNICEF is the major promotor

D. **Nutrition (aside from Vitamin A already mentioned).**

1 **Nutrition and illness** DRDRC should focus on feeding during illness, continued feeding during convalescence, compliance with feeding recommendations given by health providers (including identification of and follow-up of severely malnourished children by health providers) DRDRC should in this regard play a lead role in development of the nutrition module for the WHO/UNICEF initiative for the Integrated Management of Childhood Illness (IMCI)

2. **Anemia in children.** OMNI, PATH, DRDRC and Wellstart should coordinate efforts especially because of high mortality from anemia and the multi-faceted causes of anemia Mission staff asked specifically about the role of mother's anemia, malaria, and intestinal parasites Research may also be necessary to identify better prevention and treatment interventions

3. **Improving nutritional status during the weaning period.** Many of the programs providing food aid focus on school age children DRDRC should focus on the weaning period and the provision/acceptance of complementary foods Attention should be given to improving nutritional status as part of child survival and child development Efforts have been minimal in areas of behavioral research and the role of appetite and should be increased Except for WHO/CDR (which has the mandate within WHO), DRDRC should not devote resources to breastfeeding research and promotion, since Wellstart and OMNI are supporting them Wellstart, OMNI and Mothercare should continue to play the lead role in improving women's nutrition

4 **Micronutrients (other than Vitamin A).** A few studies on zinc supplementation indicate a need for additional research Little discussion took place on this topic but the need for prioritization of research in this area was emphasized

5 **Nutrition and Prevention.** DRDRC should coordinate its efforts with other projects in order to identify ways outside the health care system to improve nutrition in children under five Mission staff noted that the role of IEC needs to be elucidated and its effectiveness improved

E. **Integrated approaches to preventing and treating childhood illness.** DRDRC (WHO/CDR) has taken the lead on treatment and training guidelines for IMCI Research issues have been identified by WHO/CDR and should be pursued by other DRDRC components as well as JHU Some research issues have not been well articulated Organizational constraints to implementation and difficulties in changing provider behavior need more attention BASICS should play a lead role in assessments for and implementation of IMCI, including logistics of drug supplies/distribution Many governments are pushing integration at the national level, and we know it exists at the periphery USAID should facilitate integration and monitor its impact, feasibility and cost effectiveness Impact and progress could best be monitored by entities who are uninvolved in implementation (JHU, QA) JHU is conducting operations research which looks at the feasibility of the delivery of family planning and child survival interventions together in an urban setting and may field test preventive intervention packages at the community level (likely to involve collaboration with USAID's Center

for Human Resource Development, especially education) Because of epidemiological variations and country or region specific modules (such as that for nutrition) bilateral or regional resources may be appropriate

F. **Development of meaningful indicators for measuring research progress and research capacity building.** A lively discussion took place on this subject Quantitative as well as qualitative indicators are needed Many of the quantitative indicators, such as the number of peer reviewed publications, have limited value in an LDC setting, yet they are important for credibility and dissemination of results DRDRC (ADDR) should continue to take the lead here with input from foundations, donors etc

G. **The young infant.** Child survival interventions have succeeded in decreasing mortality in children under five The next generation of child survival interventions needs to focus on the first few months of life where, for example, the largest numbers of ARI deaths occur Approaches may include maternal immunization, better nutrition for adolescent girls and mothers, and better case management for the major causes of death DRDRC should focus its efforts on (1) maternal immunization (in collaboration with CVI Project) and (2) education of mothers in care-seeking behavior taking into consideration analysis of the research recently undertaken by WHO/CDR Ways to improve postpartum maternal nutrition so as to increase the nutritional value of breast milk is also important but should not be a focus area for DRDRC The Wellstart Project is supporting research in related areas

H **Introduction and impact assessment of Heat Markers for vaccine vials** Introduction including training should be facilitated by WHO/EPI, UNICEF, Rotary International, PATH, and BASICS Impact should be independently assessed in 1996 (but planned in 1995),by JHU for example, in a variety of settings Therefore, Heat Marker assessment is not an area for DRDRC to invest resources (unless JHU is incorporated within DRDRC) The Vaccine Institute in Korea should be encouraged to participate in introduction efforts

I. **Communication and advocacy.** This is a gap for most research areas There are many different levels to target, and communications and advocacy activities take time and money Bilateral donor agencies should be well versed in research results as they have easy access to published work However, implementing institutions funded by these agencies do not usually program research results in a timely manner There is considerable success in incorporating research results into global policy and at the country level where researchers have "ownership" and often have a close relationship with policy makers Mission staff and reviewers alike suggested that DRDRC enhance communication of research results to researchers and local policy makers and identify new strategies for communicating with mothers DRDRC should also consider organizing large advocacy meetings and workshops for journalists, seeking advice from the Futures Group, and designing communications for lay people (eg newspaper articles)

J. **Development of more effective training and follow-up, especially for private practitioners** Rewriting curriculum and short periodic training courses are only one

approach Medical school examinations which include child survival case management, recertification of physicians and hands-on training in the field through research were some of the other approaches discussed This area is not a priority for a research project such as the DRDRC but needs to be covered by USAID training and implementation programs

K **Water and sanitation.** The focus for DRDRC is hygiene at the household and community level Many gaps exist, especially behavioral research and the identification of feasible cost effective and sustainable interventions EHP and DRDRC should play complementary roles in this area, close communication could facilitate the transformation of DRDRC's research findings into implementation by EHP

L Sustaining immunization Considerable work is being done in this area, including a Dutch study and a strategic plan put forth by UNICEF This is an issue for implementation projects rather than DRDRC

M. **Management research.** Research concerning the factors influencing decision making at health facilities, the role of incentives and of social marketing in stimulating behavior change were perceived by the external consultants to be a major gap They suggested contacting the Futures Group, Sloan School, and HIID to define what areas could be targeted and by whom

N **Central Asian Republics** Little or no research is underway to clearly document the health problems and epidemiology Immunization has been emphasized, and known technologies are appropriately used Yet deaths from ARI and diarrhea diseases, which EPI does not greatly affect, remain high Before resources can be allocated, rational interventions must be planned and considerable baseline information should be gathered

V The Research Priority Setting Process

A Research Priority Setting by the Cooperating Agencies (Richard Cash, Jim Tulloch, and Demissie Habte)

The ADDR Project has five emphasis areas, which have evolved based on the needs perceived by staff and outside experts Research topics are selected based on recommendations of technical advisory groups, national governments, and others ADDR chooses its emphasis countries based on discussions with local experts, fact-finding missions, and USAID child survival priorities Local capacity and interest are important considerations Following the recommendations of perious evaluations, ADDR has moved from a fixed Technical Advisory Group to an ad hoc one that focuses on specific topics

Priority setting at WHO/CDR takes place within the limitations set by the Division's objectives and its budget Four research and development working groups ensure that research activities address key issues of implementation programs Commissioned

reviews and external consultations have been used to identify research priorities The Division is guided by three external advisory groups the Technical Advisory Group, a Management Review Committee, and a Meeting of Interested Parties

The ICDDR,B's mandate and comparative advantage form the basis for priority setting During the most recent exercise, a center-wide team worked with external consultants to draft a five year strategic plan, which outlined research priorities The draft plan was revised following its presentation to the Board of Trustees and again following distribution of the draft to the donor community Once every two years, the activities of each of the ICDDR,B's four divisions are reviewed formally by external consultants and board members

B The WHO Review of Priorities for Health Research and Development (Jim Tulloch)

WHO has undertaken a review of opportunity for research and development in the health sector Building on the World Bank's *World Development Report 1993 Investing in Health*, the study will identify avenues of health research and development that are good (and less good) investments and identify institutional arrangements best suited to implement the research The study will provide donors, aid agencies, health care providers, and others with an analytical tool for decision making The study is coordinated by the Directors of the WHO/CDR and WHO/TDR Programs and its total cost is expected to be about $950,000 An independent committee of 35 experts has been assembled to carry out the study, which is chaired by Dean Jamison and Kamini Mendis Three working groups have taken on different responsibilities The first working group, chaired by Chris Murray, will review research priorities for diseases, risk factors, and disabilities The second working group, chaired by Julio Frenk, will review health research priorities for households, populations, and health systems The third working group, chaired by R L Misra will review institutional arrangements for conducting the research The draft report is expected to be completed in June 1995 with a final report expected in September 1995 The degree of endorsement from WHO will be at the discretion of WHO's Director General

C Research Priority Setting by USAID (Fran Carr and Nils Daulaire)

USAID is not a public health agency However, one of its fundamental strategies for achieving sustainable development is to stabilize population growth and protect human health Emphasis will be placed on intersectoral programming, and health activities that do not support the Agency's population objectives will be at a disadvantage for funding

The struggle within USAID between global and country-specific field support activities has important implications

Global research activities which rely on central funding and long term commitment are at a particular disadvantage Upper level management sometimes lacks an understanding of the nature of research They expect and demand short term results which are not usually feasible Perceptions persist that research is a luxury afforded only to developed countries and is ridden with redundancy Some of the increased

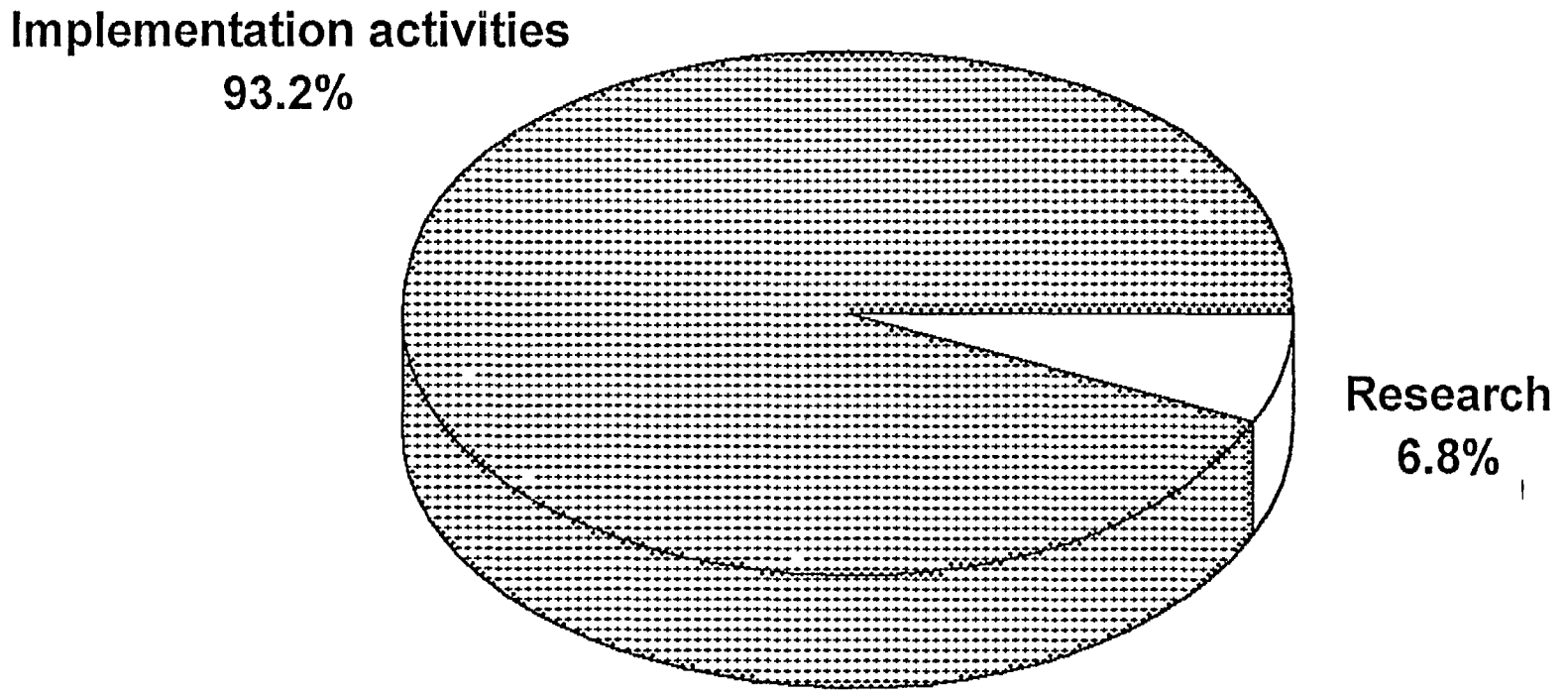
scrutiny of research reflects a trend taking place throughout the federal government - a move toward more applied, directed research

USAID will be engaged in a sector-by-sector review of research programs The intent of the reviews is to discuss accomplishments, current priorities, and future directions, all in light of current and projected budgets These internal reviews are expected to be followed by external reviews

All offices and centers in the Global Bureau will be engaged in strategic planning through March, 1995 Attention will be given to funding activities within strategic objectives It is anticipated that the role of research within each office and center will be an important issue The role of applied, long term research (which cannot be defined in advance yet is crucial for future programs) will have to be considered within this context

TABLES

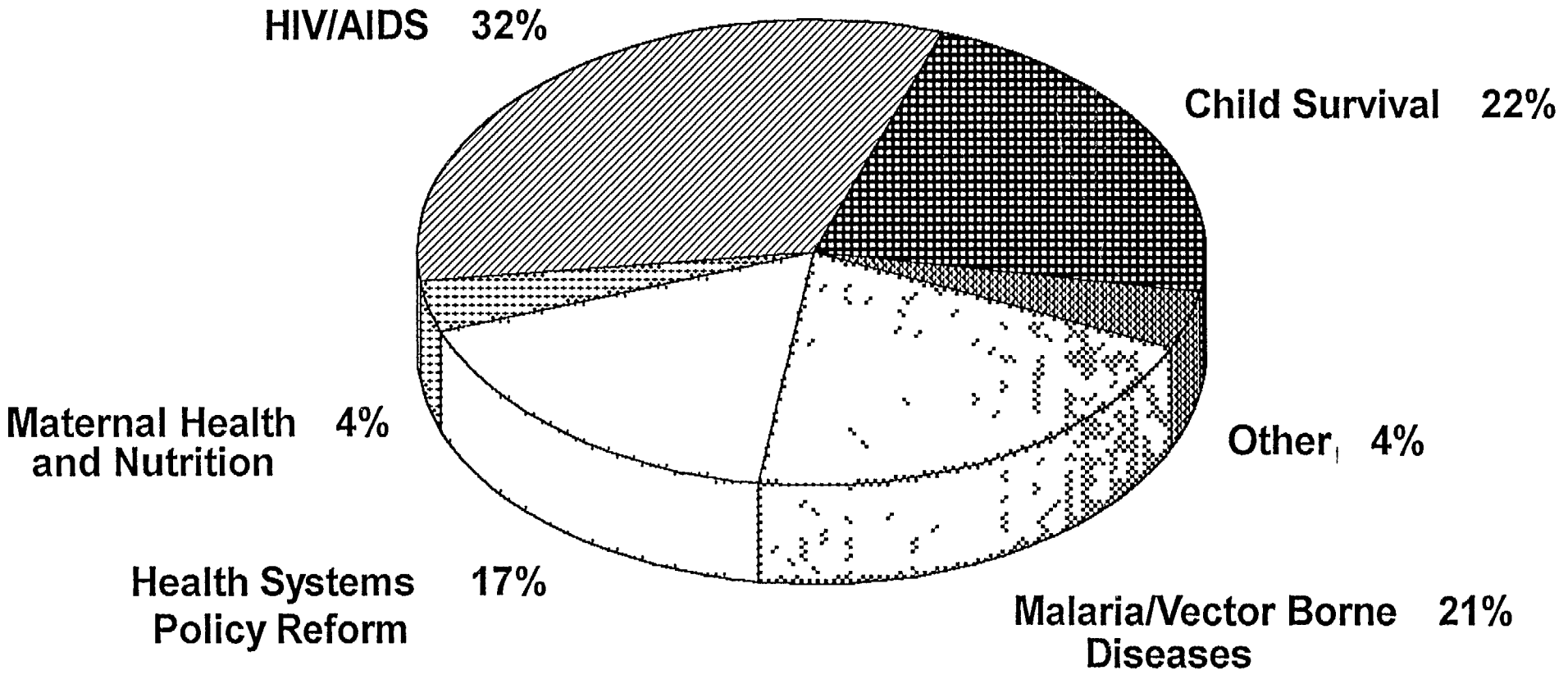
Figure 1
Research as a Percentage of Funding for Health and Nutrition Fiscal Year 1994



Note FY94 funding for health, child survival, nutrition and AIDS is $614 million with $41 8 million for research

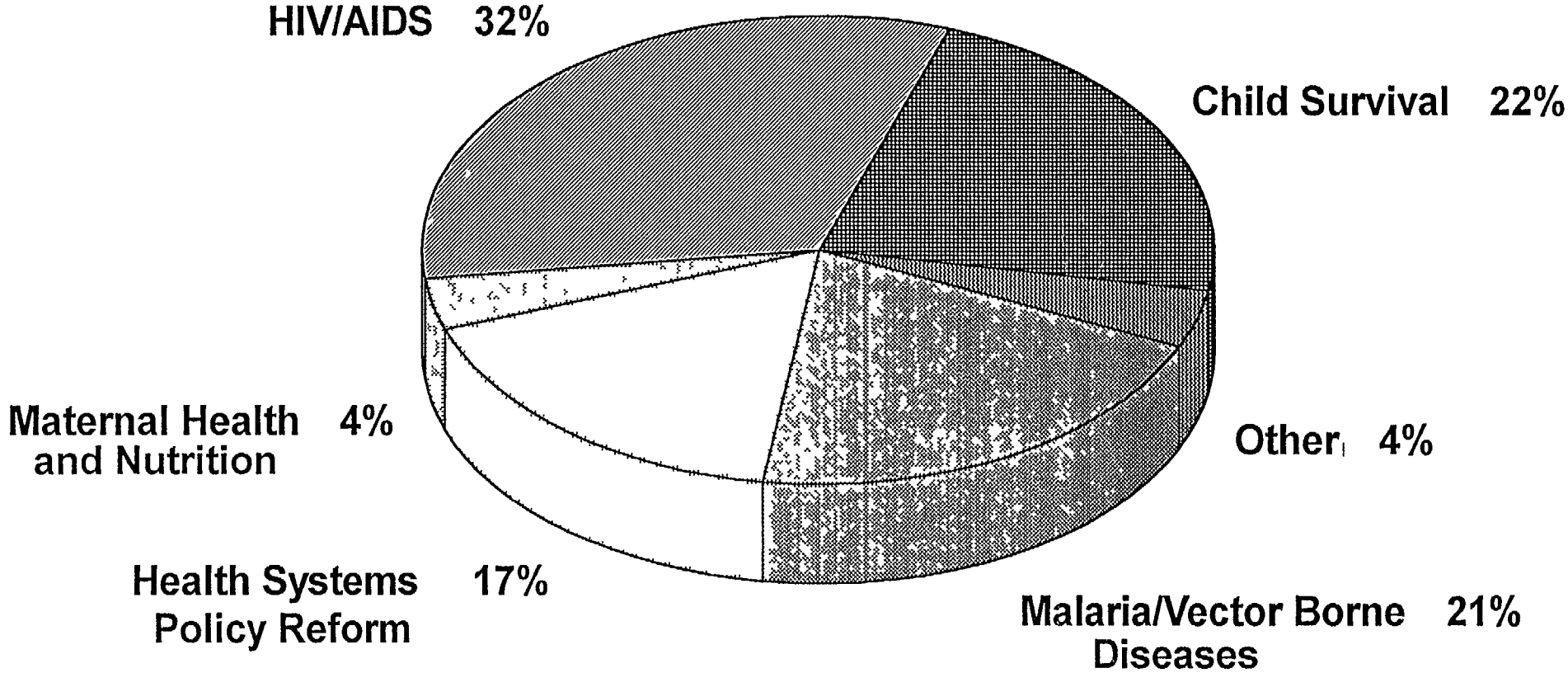
Source survey of bureaus, missions and central projects as of 2/95

Figure 2
Health and Nutrition Research Investment
Fiscal Year 1993



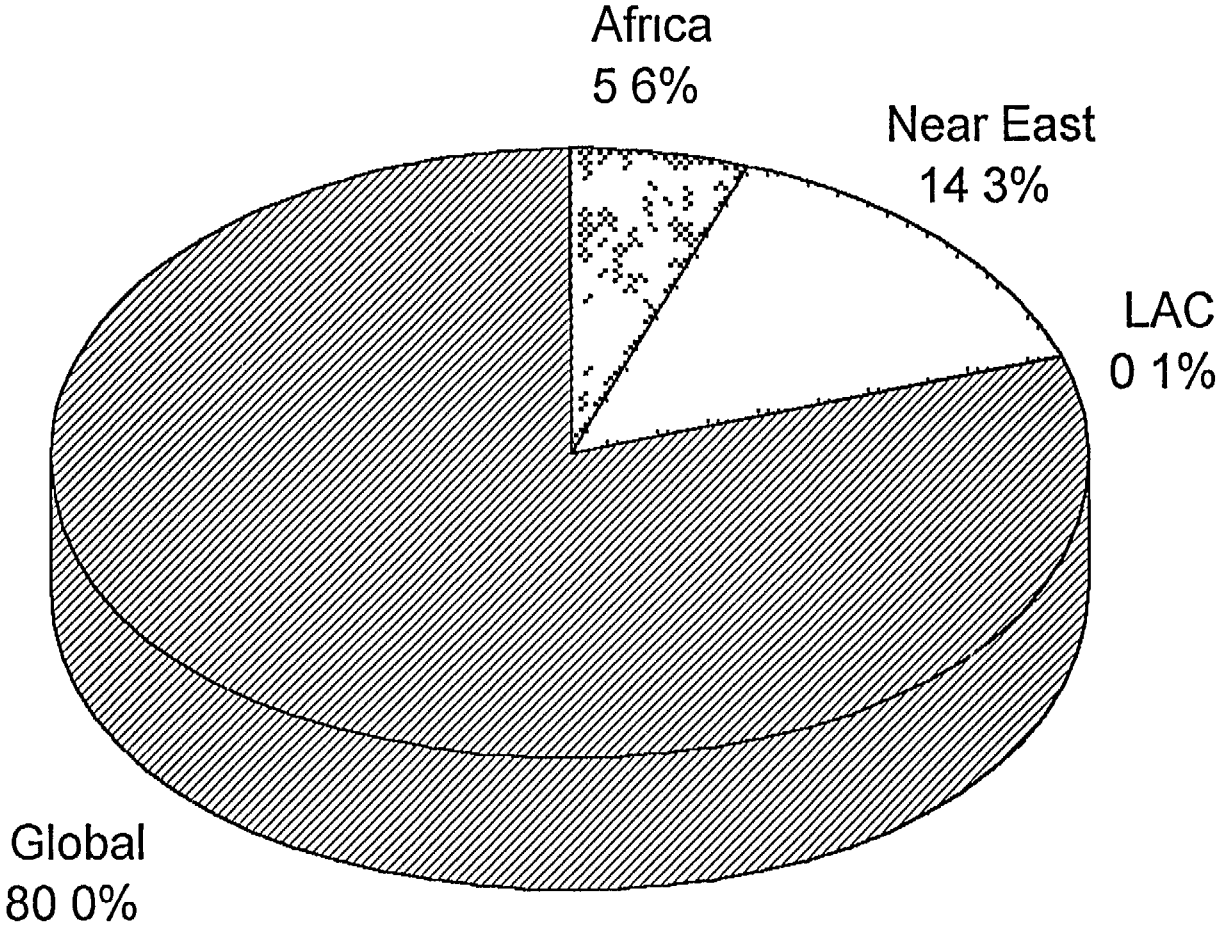
Total Funding for Health Research $91,453,000

Figure 2
Health and Nutrition Research Investment
Fiscal Year 1993



Total Funding for Health Research $91,453,000

Figure 3
Health and Nutrition Research Implemented by Bureau, FY94



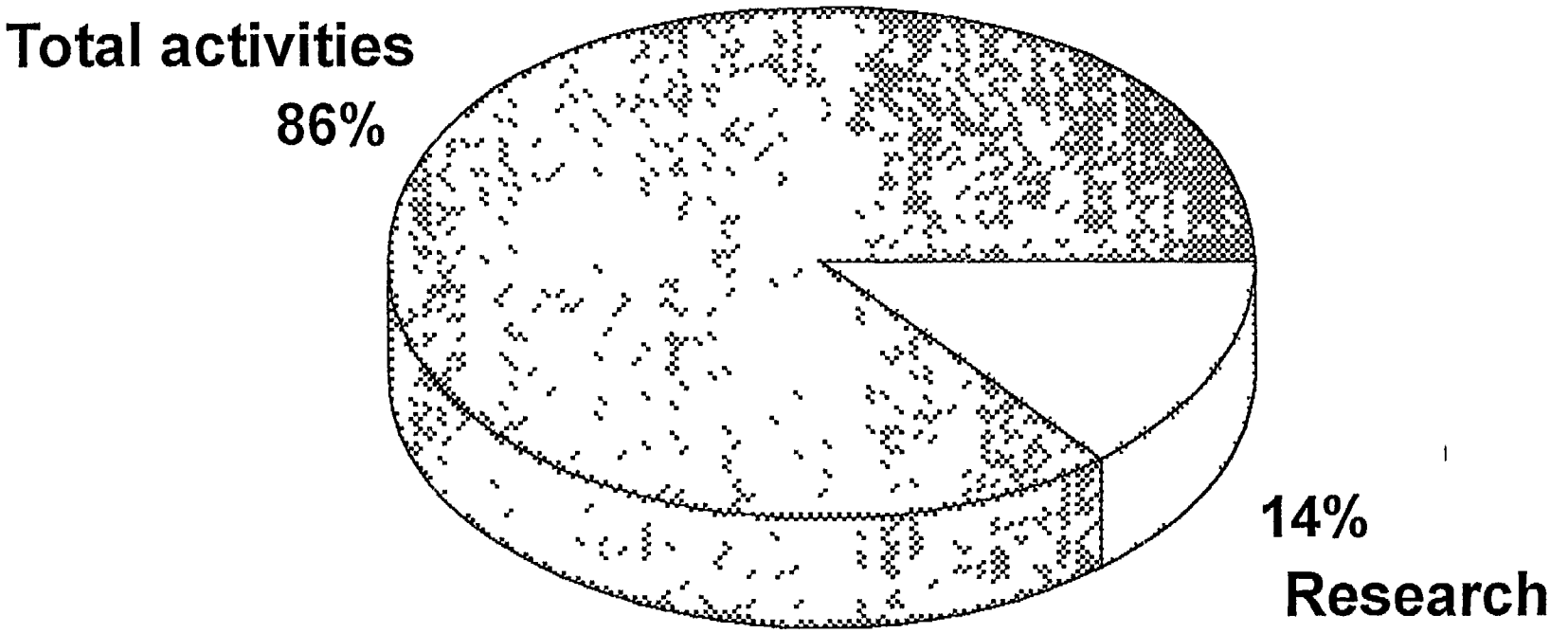
Note: FY94 total for health research is $41,852,310

Add-ons/OYB transfers are attributed to implementing bureaus

Source survey of bureaus, missions and central projects as of 2/95

Figure 4

USAID's Contribution to Health and Nutrition Research Fiscal Years 1985 to 1994

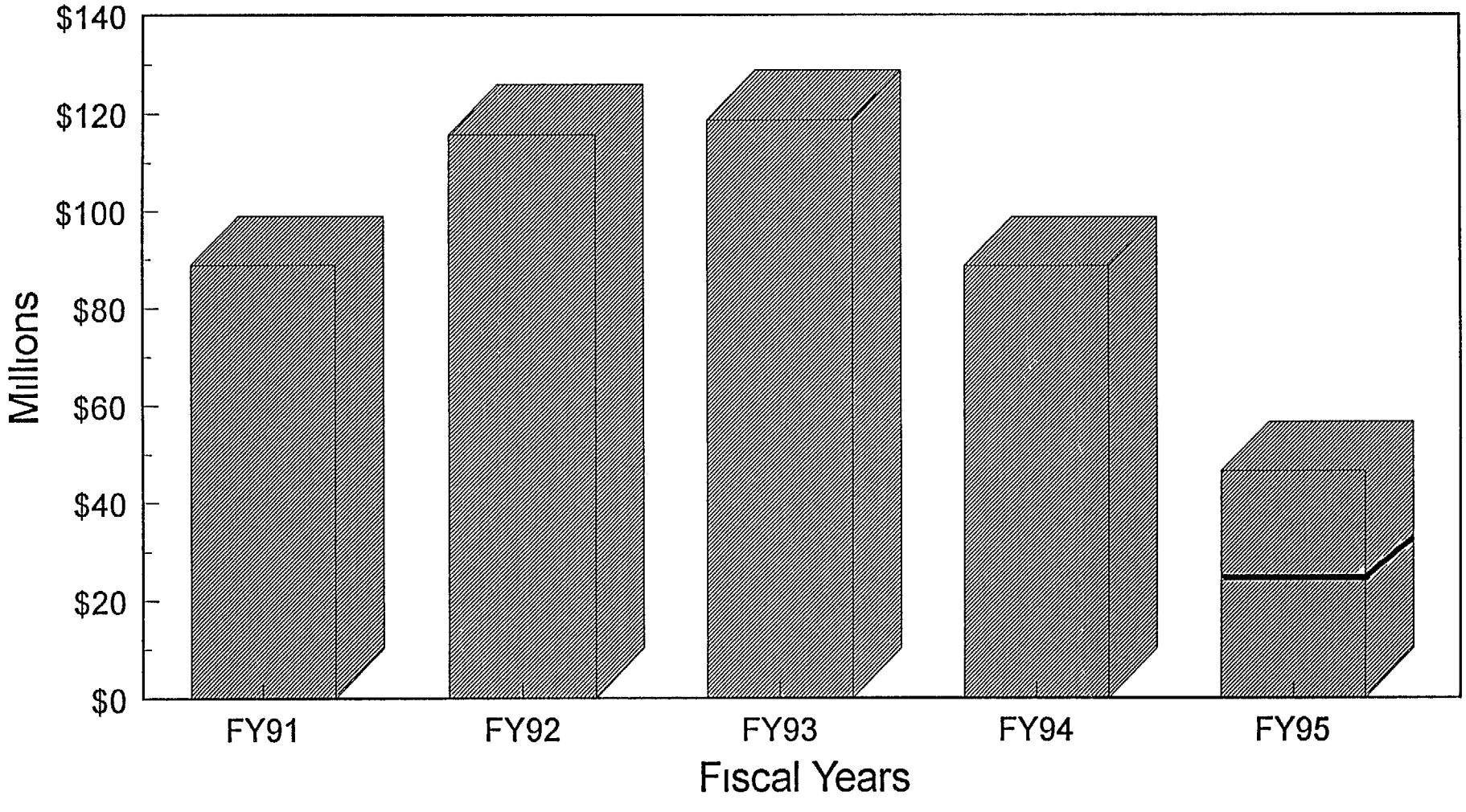


Total funding for health and nutrition activities is $4.0 billion

Total funding for research is $646.2 million

Figure 5

USAID Funding for Health and Nutrition Research

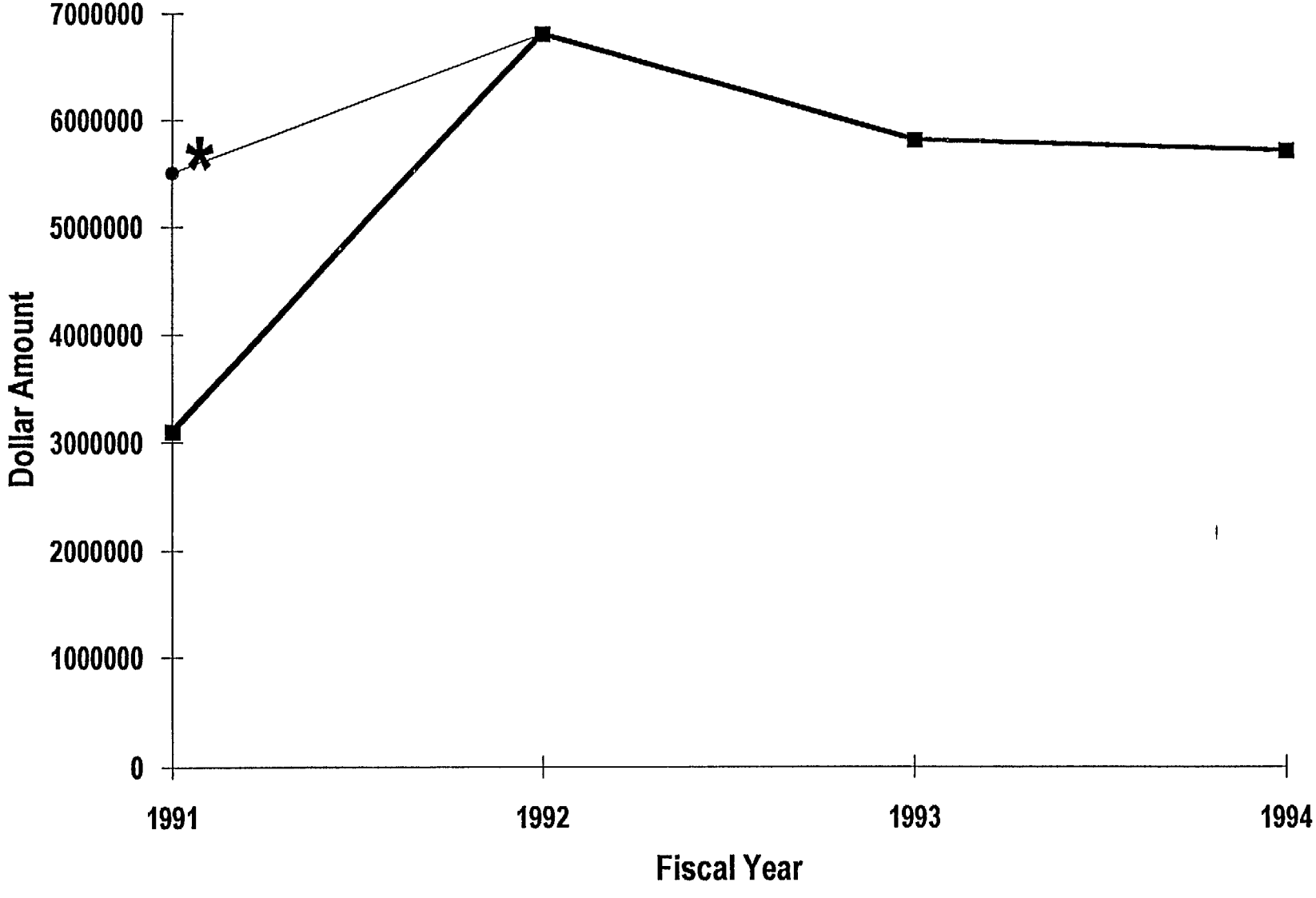


FY91-4 reported from the AC/SI System FY95 funding is shown as the requested level from 4/94, and with the resources allocated for G/PHN/HN as of 3/95 (the area below the dark line) The FY95 request is from a survey of bureaus, missions and central projects as of 2/95

Figure 6

DRDRC Project

Total USAID Obligations

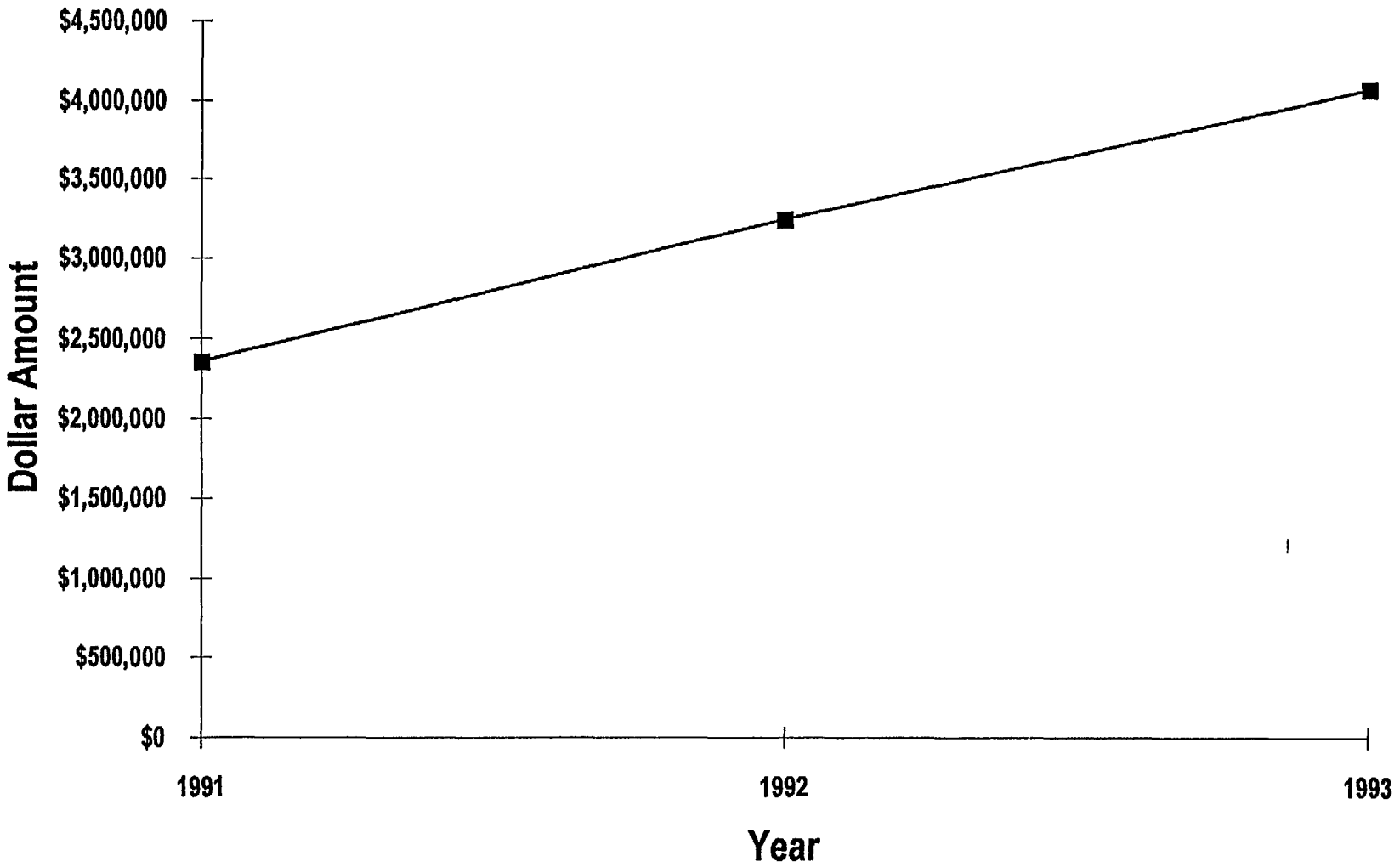


* Includes funding for ADDR although it was not incorporated into DRDRC until 1992

Figure 7

DRDRC Project

Funding for Research Grants/Contracts*



* No funding for WHO/ARI in 1991
Does not include study support costs
Includes funding for ADDR in 1991 although it was not incorporated into DRDRC Project until 1992
Includes mission add ons and OYB transfers

Figure 8
DRDRC Project
Funding for Research Grants/Contracts by Region and Developing Country in 1993

			1993 Funds
AFR	**18%**	Burkina Faso	$38,701
		Cameroon	$25,718
		Cote d'Ivorie	$81,071
		Ethiopia	$59,100
		Gambia	$77,550
		Ghana	$45,836
		Kenya	$85,380
		Nigeria	$196,139
ANE	**52%**	Bangladesh	$1,360,612
		Egypt	$55,372
		India	$193,333
		Indonesia	$57,434
		Myanmar	$4,726
		Nepal	$39,580
		Pakistan	$65,507
		Philippines	$4,950
		Thailand	$20,700
		Vietnam	$3,954
ENI	**2%**	Turkey	$60,580
LAC	**28%**	Bolivia	$18,275
		Brazil	$53,850
		Colombia	$5,000
		Ecuador	$111,673
		Guatemala	$201,760
		Honduras	$33,912
		Mexico	$20,160
		Peru	$375,780
		Venezuela	$138,093
TOTAL			**$3,434,746**

Figure 9

DRDRC Project

Funding for Research Grants/Contracts by Region in 1993

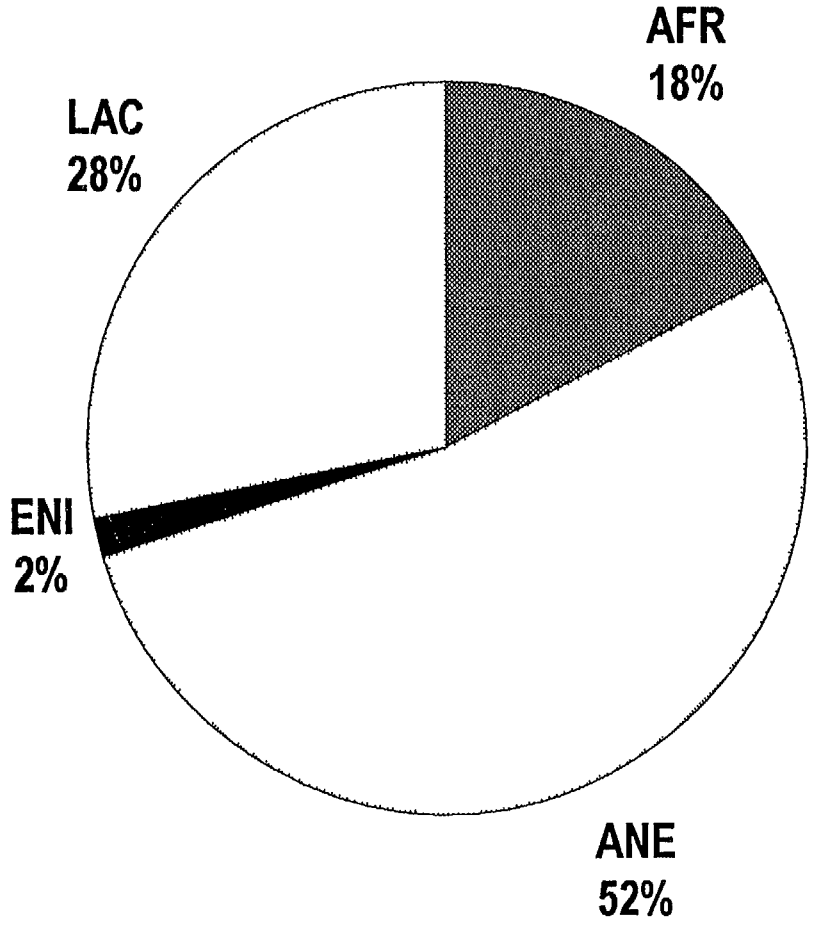


Figure 11

DRDRC Project

Funding for Research Grants/Contracts by Disease Category and Year 1991 - 1993

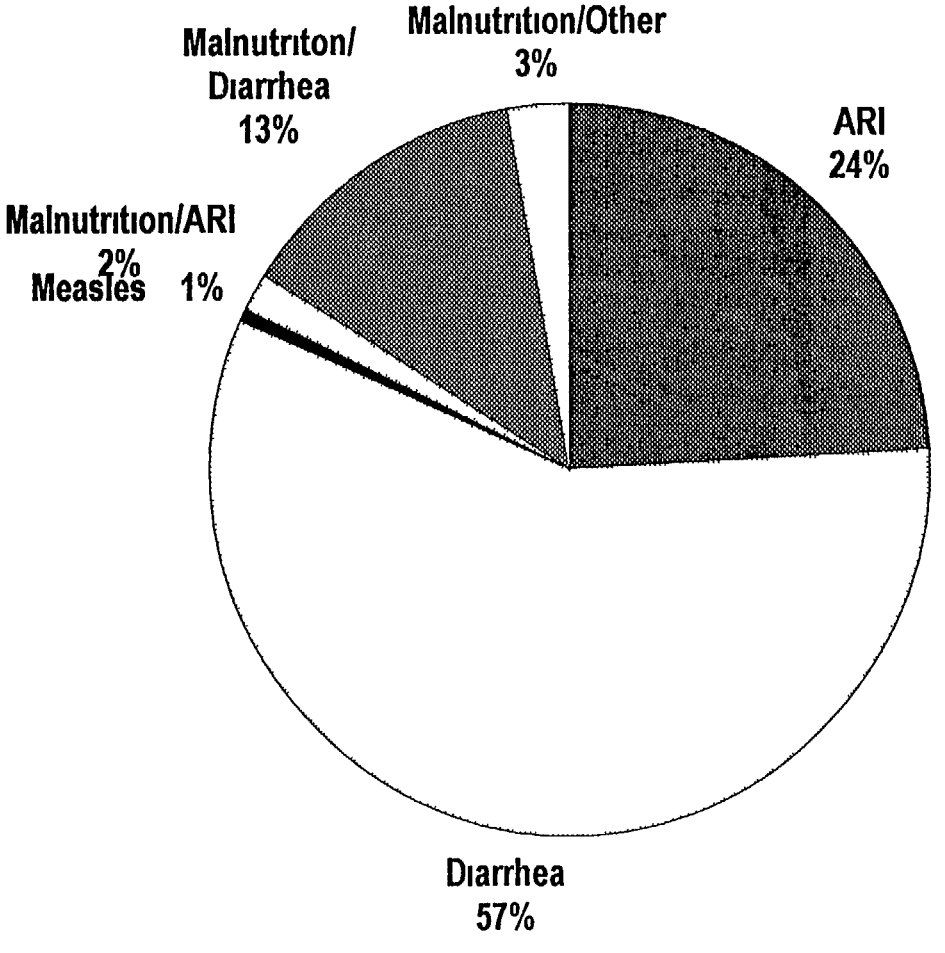
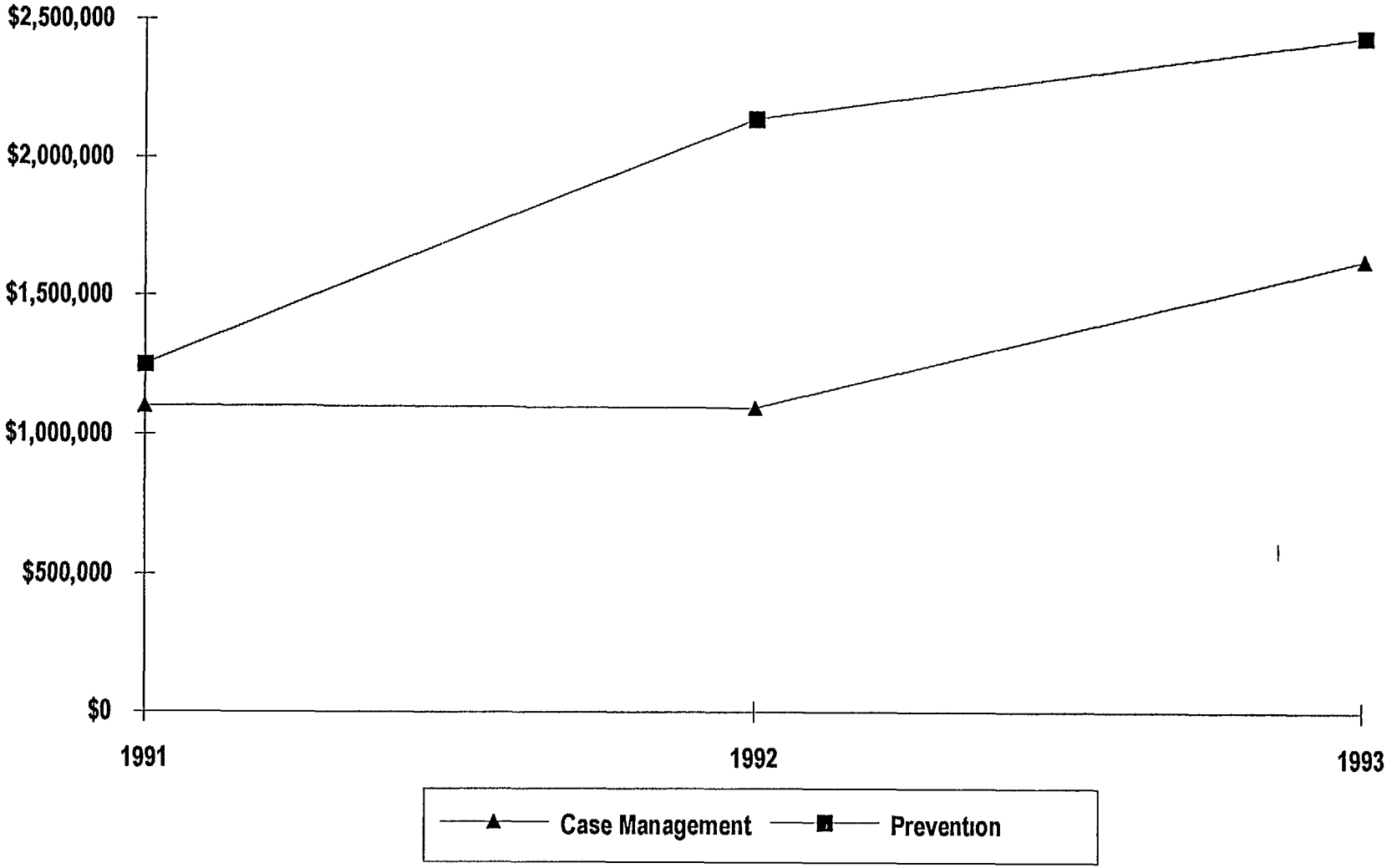


Figure 16

DRDRC Project

Funding for Research Grants/Contracts*
Case Management vs. Prevention



* Does not include study support costs
No funding for WHO/ARI in 1991
Includes funding for ADDR in 1991 although it was not incorporated into DRDRC until 1992

Figure 17

DRDRC Project

Funding for Research Grants/Contracts by Region and Developing Country in 1993

Case Management

	1991 Percent	1992 Percent	1993 Percent
WHO/ARI	0%	61%	61%
WHO/CDD	41%	21%	21%
ADDR	83%	37%	47%
ICDDR/B	29%	27%	27%

Prevention

	1991 Percent	1992 Percent	1993 Percent
WHO/ARI	0%	39%	39%
WHO/CDD	59%	79%	79%
ADDR	17%	63%	53%
ICDDR/B	71%	73%	73%

* Does not include support study costs

Appendix A

List of Participants

List of Participants
DRDRC Informal Review Meeting
October 13 - 14, 1994

Name	Affiliation
Kevin Callahan	USAID G/PHN/HN
Caryn Miller	USAID G/PHN/HN
David Senser	Reviewer
Abraham Horwitz	Reviewer
Susan Zimicki	Reviewer
James Tulloch	WHO/CDR
Demissie Habte	ICDDR,B
Richard Cash	HIID/ADDR
Jim Trostle	HIID/ADDR
Jon Simon	HIID/ADDR
Bradley Sack	ICDDR,B
Frances Carr	USAID PPC/DP
Nils Daulair	USAID PPC/SA
Al Bartlett	USAID G/PHN/HN
Paul Zeitz	USAID G/PHN/HN
Bill Hausdorff	USAID/G/PHN/HN
Melinda Moree	PATH
Sam Kahn	USAID G/PHN/HN
Frances Davidson	USAID G/PHN/HN
Tim Quick	USAID G/PHN/HN
Steve Landry	USAID G/PHN/HN
Carol Rice	USAID ANE/DR/TR
Carol Dabbs	USAID LAC/RSD
Charles Oliver	USAID G/PHN/HN
Robert Black	JHU
Fay Galloway	MotherCare
Penny Nestle	OMNI

Mission staff surveyed	
Barbara Spaid	Jakarta
Nancy Sweeney	Mexico City
Charles Llewellyn	Accra
Katherine Jones-Patron	Abidjan
Sif Ericsson	Abidjan
Lois Bradshaw	Islamabad
Ken Yamashita	Quito
Susan Brems	Lima
Patricia O'Connor	Guatemala City
Rehka Masilamani	New Delhi

Appendix B

Major Achievements and their Programmatic Implications

ADDR

SELECTED SIGNIFICANT FINDINGS FROM ADDR-FUNDED RESEARCH AND THEIR IMPLICATIONS FOR POLICIES OR PROGRAMS

1991-1994

A ARI

- In light of laboratory data showing high levels of bacterial resistance to cotrimoxazole, the drug of choice for outpatient treatment of pneumonia in Pakistan, a community based trial of the drug's effectiveness in children with suspected pneumonia was undertaken for the Aga Khan Health Services in the Northern Areas of Pakistan Cotrimoxazole was effective in 91% of pneumonia cases In addition, it was significantly cheaper than the alternative drug and had a less complicated dosage schedule

At a savings of $1 85/episode, with an estimated 18 million treatable episodes of pneumonia per year in children, the Pakistan ARI Programme will save millions of dollars and achieve higher levels of patient compliance

- In rural Sindh Province in Pakistan, primary school teachers selected and trained to be community health workers can correctly assess, classify, and manage ARI in about 80% of cases Mismanagement of cases was usually caused by miscalculating the correct dose of the appropriate drug for children at specific weights

The Pakistan ARI Programme is investigating greater use of community health workers in their Programme activities

B NUTRITION

- Previous studies demonstrated that continued feeding during episodes of diarrhea lessens the nutritional deficit of diarrhea Researchers in Mexico, Pakistan, and Peru tested locally available, inexpensive substitutes for the more expensive and less available imported soy formula fed to severely malnourished children with diarrhea The diets based on local ingredients were just as effective and safe as the soy diet (Nurko and Garcia 1993, Bhutta et al , 1994, Gastañaduy, n d), and they were significantly less expensive

- In northern Pakistan, dowdo, a locally available food for the region, was compared successfully to the kitchri diet recommended for use among children with acute diarrhea in the south (Jan et al , n d)

- An algorithm for nutritional management of persistent diarrhea among children in hospitals was successfully tested in a six country, multicenter trial co-sponsored by ADDR and WHO Modified versions of the Mexican, Peruvian, and Pakistani diets mentioned above were among those tested

The Children's Hospital in Mexico now routinely uses the local diet and has reduced its food expenditures for these children by about 75% Similarly, the local diets are also used in the Nutrition Research Institute in Peru and in the Aga Khan Hospital in Pakistan The dowdo diet has been adopted as the standard diet for children with acute diarrhea in the Gilgit District Hospital, and is being promoted as the standard diet for home treatment in the Northern Areas of Pakistan

The algorithm for nutritional management of persistent diarrhea works well in up to 80% of cases WHO will include it as part of the standard recommended treatment guidelines for persistent diarrhea in children Significant savings will be realized from using this algorithm because it involves lower food costs, reduced medication use, and reduced duration of hospital stays If the algorithm can be adapted for use in the community, additional savings will be achieved

- The National Institute of Pediatrics in Mexico developed an inexpensive and locally available diet for treating diarrhea in children who were not severely malnourished

Results were sufficiently convincing to hospital staff that the diet is now in use at the Institute, and mothers are taught how to prepare the diet for their children at home (Maulen and Brown, in press 1994) The principal investigator, supported by the National Diarrhea Control Program, is now negotiating with the Government for support to test the diet in four states

- Researchers in Peru compared two interpersonal education methods (oral recommendations with or without cooking demonstrations) to promote infant feeding and proper dietary management of diarrhea They found that both methods improved weaning diets, but the oral recommendations alone were more cost effective (Jacoby et al , 1994)

These results will help the Peruvian Ministry of Health decide what interventions to use when trying to improve infant feeding practices

- Researchers in Nigeria found that children of market women were at particular risk for diarrhea and inadequate feeding (Ene-Obong et al , 1994) They proposed a set of appropriate interventions for this group that emphasized breastfeeding and proper preparation of weaning foods

Identifying risk groups and high risk behaviors is a necessary precursor to developing appropriate interventions This study will form the basis for such interventions in this important subgroup of children at risk of diarrhea

- A study in Pakistan found that dietary intake could be a simple and inexpensive screening tool to assess vitamin A status in communities (Molla et al , 1993a) This study also recommended that hemoglobin levels not be used to predict vitamin A deficiency in Pakistan (Molla et al , 1993b)

Vitamin A deficiency is a major public health problem This study contributes to the search for inexpensive and rapid assessments of vitamin A status

- A meta-analysis of 29 clinical trials showed that most young children with acute diarrhea can be successfully managed with continued feeding on undiluted nonhuman milk, rather than the more expensive lactose-free milk formula (Brown et al , 1994)

Until this study was completed, controversy surrounded whether young children with acute diarrhea could be fed milk containing lactose, and whether milk should routinely be diluted in these cases This analysis shows that while there are small clinical disadvantages of giving undiluted milk to young children with diarrhea, there are large nutritional benefits

- Amylase can be added to increase the energy density of rice-based ORS (so that rice-based ORS can better alleviate the nutritional wasting associated with diarrhea) However, a study in Guatemala found high rehydration failure rates at a 15% rice/amylase concentration, and suboptimal results at a 10% rice/amylase concentration (Vettorazzi et al , 1993) Because of the preparation expense and time, and the unacceptable failure rate, rice-based ORS treated with amylase is not recommended for general use to treat dehydration

Amylase does not appear to be effective in increasing the energy density of rice-based ORS without lessening the ability of rice-based ORS to rehydrate

C CASE MANAGEMENT AND PRESCRIBING PRACTICES

- Studies investigating prescribing practices showed that professional knowledge often did not predict appropriate behavior, and that training alone was unlikely to create major sustained behavioral changes among prescribing professionals The studies also showed dramatic differences between reported and observed practices, and between private and public practice (Gani 1991, Igun 1994a and 1994b, del Aguila and Brown 1993, Paredes 1994, Santoso 1994, Guiscafre et al 1994, Gutierrez et al 1994, Nizami et al 1994, Perez et al 1994)

- Educational and managerial interventions in a Mexican Social Security (IMSS) clinic significantly reduced the proportion of children who received antibiotics and antidiarrheals, and increased ORS use These changes have lasted more than 18 months after the intervention ended (Gutierrez et al , 1994) Medication compliance improved among patients in the intervention group even though this was not an explicit objective of the intervention (Bronfman 1993) A second study undertaken by the IMSS extended the methods to 17 clinics from both the IMSS and the Mexican Ministry of Health, and looked both at diarrheal diseases and ARI Results from this randomized controlled trial of clinics were also successful (Gutierrez et al , 1992), with medication costs decreasing by 36% and medication waste due to noncompliance and overprescribing decreasing by 51%

- ADDR studies of doctor-patient interaction demonstrated that the mean duration of clinical interviews ranged from 2 $\pm$ 1 minutes for general practitioners in Multan, Pakistan and 3 $\pm$ 2 minutes in Karachi, Pakistan, to 9 minutes for physicians in the IMSS system in Mexico

Interventions to change professional prescribing practices should include managerial and/or legislative components, as well as training Such interventions must be carefully tested and should not measure outcomes only through professional self-report Interventions combining training and management techniques can change physician behaviors for significant periods of time and can act indirectly on patients to improve their treatment compliance

In Mexico, the Minister of Health took an active interest in these results The IMSS is now implementing a new diarrheal disease treatment program in 12 Mexican states

In other countries such as Pakistan, little was known about the practice and work incentives of private physicians, and few interventions were directed toward them This research prepared the groundwork for such interventions For example, new interventions aimed at physicians should take account of the constraints limiting encounter times Adding even three minutes of extra work to a general practitioner in Pakistan potentially halves the number of pediatric patients who can be seen, with dramatic effects on potential earnings

D PREVENTION

- Household surveys and observations of the hygiene practices among residents of Peruvian shanty town dwellings identified a number of defecation-related behaviors which posed higher risks for diarrhea (Yeager et al 1991, Huttly et al 1994) A study in Thailand found that practices related to personal hygiene and improper use of ORS were important risks for dehydration from diarrhea (Arunee et al , 1992) A study in Nigeria found that food handling was not as important a risk for diarrhea in an urban population as were various behaviors related to defecation and waste

disposal (Ekanem et al , 1991) An intervention trial based on these results will be completed by the end of 1994

The successful development of hygiene interventions requires assessing risks, describing prevalent behaviors, establishing the determinants of these behaviors, and then assessing the likelihood of changing them These studies covered most or all of these four important stages

- In Indonesia, local religious leaders and Koran reading groups were successfully trained to disseminate health information about proper preparation of drinking water (Nurhayati et al , 1994)

An earlier study by this group had identified a particular habit (mixing boiled and unboiled water to prepare drinks) as posing especially high risks for diarrhea This study shows the value of using locally appropriate channels to convey important health education messages

E CAPACITY-BUILDING

- Important research and proposal-writing skills have been developed in a dozen countries through a flexible program which combines focused technical assistance with financial support

When research is conducted in developing countries, it fosters a problem-solving culture However, programs supporting researchers in developing countries must respond to structural constraints ranging from problems in acquiring computers or literature to limitations on researchers' job incentives and opportunities for collaboration A program adapted to the local academic and political environment, combining workshops, consultant assistance, and learning by experience, can overcome many of these constraints

- ADDR has developed proposal development and data analysis workshop manuals in English, French, and Spanish It has included local consultants in its workshops and shared its workshop methodology with other donors and research organizations ADDR grantees in Indonesia, Pakistan, Peru, and Ecuador have held their own proposal development and data analysis workshops following their participation in ADDR workshops

When research is conducted in developing countries, it also builds indigenous capacity for responding to rapidly changing health problems

- Together with other donors, ADDR is developing evaluation indicators for research capacity building

ICDDR,B

- Hyper-immune bovine colostrum was shown to reduce the severity of rotavirus diarrhoea in infants and young children

Rotavirus diarrhoea is one of the commonest causes of morbidity and mortality Because no specific anti-viral treatment exists for this condition, treatment with hyper-immune bovine colostrum opens an immunologic approach to the management of this disorder

- Zinc supplemented to undernourished children was found to reduce duration and severity in acute diarrhoea, and in persistent diarrhoea was shown to accelerate nutritional recovery

Zinc supplementation should be considered as an important adjunct to the management of diarrhoeal disease in malnourished children

- Intensive feeding over a two week period with a high calorie, high protein diet of infants and children with shigellosis resulted in rapid catch-up growth in association with marked increases in the blood level of growth-human-like substances

Shigellosis is an important cause of determination of nutritional status in infants and children Intensive feeding should be practiced to prevent malnutrition following shigellosis

- Ciprofloxacillin and mecillinam were found to be effective against infection with Shigella while cefixime and oral gentamicin failed to have satisfactory cure

Resistance to commonly used antibiotics occurs in Shigella dysentery, and new drugs have to be developed ahead of the development of resistance to drugs in current use This information provides a therapeutic guide to health professionals in Bangladesh and the region

- The addition of amylase (prepared from germinated wheat) to cereal and legume based weaning diet was shown to reduce the viscosity of the gruel and increase the energy density Such a mixture resulted in a significant increase in nutrient and energy intake in infants and children suffering from acute watery diarrhoea, acute shigellosis, persistent diarrhoea and protein-energy malnutrition

The demonstration that the use of amylase enriched cereal flour significantly increase nutrient intake during the acute phase of the disease in young infants, and that a high energy, protein diet given for a brief period during acute shigellosis results in significantly enhanced linear growth, has re-enforced and heightened the importance of feeding during diarrhoea to counter the nutritional consequences

- Pregnant women immunized with a presently licensed pneumococcal vaccine were

shown to transfer high levels of antibody to newborns and up to 14 weeks of age

The above information may lead to new, improved strategies for the protection of young infants (under 4-5 months of age) against life threatening pneumococcal diseases (that account for as much as 20% of the deaths in this age group)

- Supplementation of mothers with high doses of Vit A soon after delivery was shown to result in significant reduction of mortality in breast-feeding infants under 6 months of age

Vitamin A deficiency is usually considered a problem in older infants and children. However, it is now becoming recognized that infants under 6 months of age also suffer from the deficiency and the subsequent effects Maternal supplementation offers a safe and effective way of ensuring adequate Vit A status in young infants Maternal supplementation and breast-feeding promotion are powerful strategies for protection of infants in the first six months of life

- Handwashing using mud or ash was found to be nearly as effective as soap in reducing bacterial contamination of hands after defecation

Handwashing using mud or ash is an effective and practical technique of handwashing where soap is not available

- Administration of high doses of Vit A to young infants along with commonly given immunizations during the first six months of life was associated with a significantly increased rate of side effects as manifested by bulging fontanelles

This information has led to re-thinking of policy recommendations world-wide on the Vit A supplementation in early infancy It also led to a large multi-center trial of safety of Vit A administration in this age group

- The decline of levels of measles antibody in young infants was found to be rapid with no protective levels at 4 months of age in the great majority of infants

The above finding support strongly previous contentions that measles vaccine should be offered much earlier than 9 month of age

- Measles immunization reduces risks of mortality by as much as 46%, and resulted in significantly improved survival chances not just for infants under 12 months (the primary target group in current immunization programs) but for all children vaccinated up to 36 months of age

The results of this study provide unequivocal evidence for the importance of measles vaccination in reducing childhood mortality in developing countries, and indicate extending the target age range for measles vaccination coverage to at least under 2 years of age

- Vibrio cholerae 01 were shown to be present in the mucilaginous sheath of a blue green algae present in natural aquatic environment

This demonstration will help explain the patterns of survival of vibrios in the environment, and indicate that the natural reservoir of Vibrio Cholerae is the aquatic environment (rather than humans), and point to new directions for the global eradication of the disease

- Vibrio cholerae 0139 was identified as a new pathogen causing a disease identical to cholera caused by 01 The organism was characterized and its clinical and epidemiological feature identified

The rapid identification of a new emerging threat confirm that this is possible when infrastructure and research capabilities exist in areas where such threats occur In addition, the rapid identification of this organism helped to alert the international community to the emergence of a new threat of disease The development of a diagnostic test enabled the diagnosis of the organism as it spread around the world The clinical and epidemiological characterization provided information on management and control to areas so affected The microbiological characterization of 0139 vibrio along with the epidemiological information has contributed to the development of the new generation of cholera vaccines (both killer and live) that will be protection against both 01 and 0139

- New diarrhoeal pathogen enterotoxigenic Bacteroides fragilis, Hafnia alvei and Providencia liqufac--- recognized and characterized

Knowledge of new biological agents will contribute to the control and management of diarrhoeal diseases

- Safety and immunogenicity testing of a killed whole-cell candidate vaccine of Enterotoxigenic E coli was successfully carried out in adult volunteers

This will lead to the eventual field testing of vaccines against ETEC, that are potentially of great importance in controlling diarrhoea

- Assays have been developed to identify pathogenic strains of Entamoeba histolytica.

This had led to the development of a monoclonal antibody-based strip ELISA (in collaboration with the University of Virginia) for rapid detection of pathogenic forms

Current diagnostic methods do not discriminate pathogenic from non-pathogenic forms This test will improve diagnosis, target treatment to cases requiring it and save money by preventing unnecessary use of drugs for treating amoebiasis

- Following a devastating cyclone in April 1991, a study conducted by ICDDR,B scientists showed the most of the water purifying tablets (WPT) available had lost potency and their effectiveness was uncertain. In addition, a number of other problems associated with water purification programmes based on WPT's were

described

These finding suggest that the use of WPT's during disaster response should be significantly modified

- The Centre has developed methodologies and established procedures for rapid and effective responses to diarrhoea epidemics This capability was shown to be critical, unique and effective during the recent cholera epidemic amongst Rwandan refugees in Goma, Zaire, and was in stark contrast to ineffective, often harmful and ill-formed response of several other NGO's operating at the same time The ICDDR,B team was able to persuade them to adopt effective measures

The Centre's model for response to diarrhoea epidemics should be widely adopted by agencies involved in disaster relief, and the Centre can play an important role in developing global capability in the management of cholera epidemics

- The Centre contributed to the development of an appropriate diet for the management of persistent diarrhoea based on understanding of the pathogenesis of the disease This later became the basis of the diet used in successful large multi-centre trial

The use of such a diet will save many lives

- The Centre has conducted several training courses and hands-on experience to develop research skills of professional interested in health research coming from a number of developing (and developed) countries It has also provided research fellowships on a long term basis to a smaller number

This will be expected to contribute to research capacity building and/or strengthening in developing countries

- The Centre hold several workshops, seminars and conferences, to which individuals from Bangladesh as well outside were invited, for the purpose of disseminating its research findings Centre staff also presented their works at international conferences

This will assist the translation of research findings to policy and action

- Centre has developed institutional linkages with a number of academic and research institutions within the United States as well as in Europe, Canada, Australia and Asia.

These linkages have been mutually beneficial They have helped resolution of research issues, helped in training of staff and promoted collaboration in many other ways A recent example is the collaboration with scientist in nearly ten countries to identify and characterize V cholerae 0139

WHO/CDD

ACHIEVEMENTS OF THE CDD PROGRAMME AND THEIR PROGRAMMATIC IMPLICATIONS

- Breastfeeding was identified as of particular importance in the prevention of shigellosis among young malnourished children The risk of shigellosis was found to be 10 times greater during the first 3 months after cessation of breastfeeding (among malnourished children in Bangladesh)

  Shigellosis is a significant contributor to childhood diarrhoea These research findings confirm the importance of prolonged breastfeeding and that mothers of malnourished children merit particular attention for breastfeeding counselling

- Pacifier use was found to be associated with increased risk of early termination of breastfeeding

  Pacifier use can serve as an indicator of children whose mothers should receive breastfeeding counselling Health education messages should discourage pacifier use

- Lactation management training was shown not to increase trainees knowledge on breastfeeding but to improve practices at the health facility level and the duration of breastfeeding at the community level

- Lactation counselling clinics were shown to be effective in increasing the prevalence of exclusive breastfeeding at the community level

  These findings, showing that health workers can be effectively trained in breastfeeding counselling and that it can have an impact on practices, justify the Programme's investment in this type of training The Programme's training course for health workers on breastfeeding counselling, completed in 1993, should be widely used

- Vitamin A supplementation was associated with reduction in the incidence and duration of severe diarrhoea

  This finding supports the promotion of vitamin A supplementation in children over 6 months of age and of Vitamin A rich foods

- Three sets of hygiene behaviors were identified as of key importance for promotion in the prevention of diarrheas sanitary disposal of faeces, handwashing, and maintaining drinking water free from faecal contamination.

  Hygiene promotion efforts should give priority to these 3 behaviors rather than trying

to cover all areas of hygiene

- The importance of early feeding in the treatment of diarrheas confirmed by completed studies

  This finding supports the policy of continued feeding during diarrhoea promoted by WHO and most national CDD programmes

- Supported studies showed that for infants under 6 months of age with diarrhoea whose only food is animal or formula, the milk or formula normally given does not need to be diluted and should be provided in full strength as soon as dehydration has been corrected A review of all clinical trials on feeding milk during diarrhoea has confirmed the WHO's recommendations to continue giving undiluted milk to infants and children with diarrhoea

  The WHO case management guidelines have been simplified by removing a recommendation to dilute milk feeds for children under 6 months of age National CDD policies should also be modified

- The key importance of increasing the energy density of weaning foods as a means to improve energy intake was demonstrated in a project from Peru

- Viscosity reduction by the addition of amylase was shown not to improve the energy intake of young children in Jamaica Its only advantage was a shorter time spent feeding

  These findings demonstrate that increasing the energy density of complementary foods is an effective way to increase energy intake and that this can probably be achieved by promotion of semi-solid cereal foods without amylase-induced reduction in viscosity

- The first version was developed of a Focused Ethnographic Study protocol to generate descriptive data on beliefs and practices related to diarrhoea for use in the implementation of national programmes

- A training guide that aims to provide health workers' the necessary skills to effectively advise mothers on the treatment of diarrhoea was developed and integrated into CDD's Clinical Management Course

- Packages of training materials were also completed and printed for improving teaching on diarrhoea in medical schools, for similar efforts in basic health worker training of other kinds, for changing the prescribing practices of pharmacists and drug sellers and for self instruction in diarrhoea case management

These materials add to the wide range of practical tools developed for use in national CDD programmes and support a strategy institutionalizing effective CDD training of health workers

- Improvements in diarrhoea case management in North East Brazil were identified as a major contributor to the reduction of almost 60% in diarrhoea mortality in infants observed in the region between 1980 and 1990 Other potential contributors for the decline such as, improvements in nutritional status, water supply, vaccine coverage and breastfeeding duration could only account for approximately one-third of the observed reduction

  The findings of this study can be used to advocate with donors and developing country decision makers the effectiveness of the promotion of correct diarrhoea case management

- The routine use of antimicrobials has been identified as not effective for the treatment of persistent diarrhoea

- An algorithm for the management of persistent diarrhoea in hospitalized children was evaluated in a multicentre trial involving 6 countries The overall success rate of this algorithm was found to be close to 90%

  The algorithm can now be made available for use, assessed under usual health facility conditions and incorporated into WHO and national programme diarrhoea treatment guidelines that do not include the routine use of antibiotics for persistent diarrhoea

- All Programme-supported studies on rice-based ORS were completed and analyzed The results demonstrate that rice-based ORS does not offer any advantage over WHO-ORS solution in the treatment of non-cholera acute diarrhoea when feeding is continual following rehydration Rice-based ORS is superior, however, for the treatment of cholera

- ORS solutions of low osmolarity have been shown to reduce stool output and the proportion of treatment failure, in comparison with standard ORS, when used for infants and young children with non-cholera diarrhoea

  These studies provide the basis for a formal consideration of whether either rice-based or low osmolarity ORS have sufficient advantage over standard ORS to be considered the preferred treatment for cholera or acute non-cholera diarrhoea.

- An evaluation of the efficacy of tetravalent rhesus-human rotavirus vaccine was completed in Brazil and a trial involving a higher dose of the vaccine was started in

Venezuela

Results of the Venezuela trial will help considerably in defining whether the tested vaccine has potential as a public health tool in developing countries

- Efficacy trials of Ty21a live oral typhoid vaccine were completed in Chile and Indonesia.

  These studies established a safe and effective immunization regimen for this vaccine They also led to the acceptance for licensure of the vaccine by the USFDA, which will facilitate acceptance of the vaccine in other countries

- Safety and immunogenicity of the single dose parenteral Vi vaccine for typhoid fever, already proven effective for older children and adults, was determined in infants and young children in Indonesia The vaccine had reduced immunogenicity in children below 15-18 months

  The results indicate the vaccine would not likely be fully effective given to infants within the EPI Programme This gives encouragement to evaluating a Vi-conjugate vaccine in this age group

- The safety and immunogenicity of the killed oral cholera vaccine, WC/B, developed in Sweden has been confirmed in Latin America

  These studies were required before evaluation of the vaccine's efficacy in Latin America would be possible Efficacy trials are now under way in Peru

- A safe and immunogenic dose of the live oral cholera vaccine, CVD 103 HgR, was established for children and adults in developing countries Based on these, the first trial to determine efficacy of the vaccine was initiated in Indonesia

  The results of the fields trial will be critical in determining whether this promising vaccine is effective under field conditions

WHO/ARI

Antimicrobial susceptibility

Four field tests of the antimicrobial susceptibility manual were carried out (Egypt, Pakistan, Thailand, Vietnam)

A study on the relationship between laboratory resistance to cotrimoxazole and its clinical efficacy in treating pneumonia completed Despite extensive laboratory resistance, cotrimoxazole may still lead to adequate treatment failure rates in children with pneumonia while failing more often in the treatment of severe pneumonia.

Research studies have developed or evaluated several laboratory method simplifications

Goats' blood works as well as sheep, horse

Improve transport media for pneumococcal isolates

Simple lyophilizer (without freon or dry ice)

Severely malnourished children

As in well-nourished children, S pneumonia and H influenzae remain the most common organisms causing bacterial pneumonia in severely malnourished children but the proportion of pneumonia caused by gram-negative organisms and tuberculosis is higher

Respiratory rate threshold for detection pneumonia needs to be lower in severely malnourished children

Family behavior related to pneumonia recognition, care seeking and treatment

The ARI Focused Ethnographic study (FES) and workbook were completed after extensive field testing

A meeting in May 1992 summarized the experience in the use of
FES data in national programs

Example of FES results Focused Ethnographic Study in North West Frontier Province, Pakistan, revealed the interplay of logistic and financial problems with social relations in the household, and cultural beliefs as factors that lead to delay seeking care for a child with signs of pneumonia. While fathers are not primary care takers, they are the primary decision makers about when and where a child should be taken for care. Financial and logistic problems of getting care strongly influence their decisions but cultural factors are

also important Traditionally, a child with fast or difficult breathing is not taken out of the house during the initial two or three days of this condition for fear that "open air" will exacerbate the problem, and that the child will die

Oxygen

Preliminary results from oxygen administration studies suggest that most children hypoxamic from pneumonia can be adequately oxygenated with nasal cannulae which are less likely to cause serious complications

Laboratory standards established for oxygen concentrators and field testing initiated in developing countries

Prevention

Preliminary results of the pneumonia prevention review suggest high priority be given to studies on Hib and conjugated pneumococcal vaccine and indoor air pollution

Review and meta-analysis of all available field trials on Vitamin A supplementation suggest no beneficial impact on non-measles-related pneumonia deaths and suggest inadequate safety data to proceed with recommendations to supplement infants less than 6 months of age

Hib vaccine trial initiated in early 1993 in the Gambia

Please indicate whether the information you have provided corresponds to calendar year(s) or US government fiscal year

Calendar year

Appendix C

List of Institutional Collaborations

ADDR

Total National = 3
Total International = 8

Non-Grant Related Technical Assistance

Support for ICDDR,B tech assistance to Ministry Public Health, Ecuador, May 1991 I C
Technical assistance to Peruvian Ministry of Health, Lima, March 1992 I C
Technical assistance to Ecuadorian Ministry of Public Health, Quito, April 1992 I C
Technical assistance to the Bolivian government, La Paz, September 1992 I C
Technical assistance in cholera for the Peruvian government, Lima, Nov 1993 I C
WHO-sponsored Focused Ethnographic Study of ARI Training Workshop, Douala, Cameroon, March 29 - April 4, 1993 I

Total National = 0
Total International = 6

3

Technical Training for ADDR Research Teams

Lab training in zinc assay methodology, advanced statistical training in regression and logistic regression techniques, Davis, CA, June 1994 I
Training in breast milk volume measurement techniques using radioisotopes, Baltimore, Maryland, May 1994 I
General training sessions on statistics/epidemiology for research teams supported by ADDR, Karachi and Lahore, April 1992 N
Training on detection of toxin-producing organisms causing hemolytic uremic syndrome, Aga Khan University, Lahore, May 1992 N
Cost-effectiveness data analysis exercise, South Hadley, MA, October-November, 1994 I

Total National = 2
Total International = 3

Multicenter Trials

Multicenter, Six-Country Evaluation of a Treatment Algorithm for Persistent Diarrhea, Peru, Mexico, Pakistan (funded by ADDR) India, Bangladesh, Vietnam (funded by WHO/CDD), 1991-1993 I PD
Evaluation of a Strategy for Improving the Treatment Prescribed by Primary Health Care Physicians of a District of Mexico City, for Diarrhea and Acute Respiratory Infection (collaboration between IMSS and Ministry of Health of Mexico), Coyoacan sanitary district, Mexico, 1991-1993 N

Total National = 1

Total International = 1

Other Collaborative Efforts

UNICEF/ADDR University-Community Linkages Project (Essential National Health Research), Nigeria, 1994 N

Mexico CDD Program Review (collaboration between AID, UNICEF, PAHO, Ministry of Health of Mexico), Mexico, September 1994 I

Research/Policy Case Studies, Mexico, September 1994-June 1995 I

Evaluating Efforts to Build Research Capacity (collaboration between ADDR, AID, IDRC, INCLEN/McMasters University, WHO/TDR, WHO/HRP), Cambridge, September 1994-September 1995 I

Pakistan Medical Research Council (ENHR activities), Pakistan, 1992-1994 N

UNICEF/Pakistan-ADDR/Pakistan co-funded meetings & workshops N

UNICEF/Nigeria-ADDR/Nigeria co-funded meetings & workshops N

UNICEF/New York-ADDR/Cambridge co-funded conferences I

Total National = 4

Total International = 4

* Of the above activities, 4 were undertaken as part of the Persistent Diarrhea algorithm, and 5 were undertaken as part of cholera technical assistance

ICDDR,B

LABORATORY SCIENCES DIVISION

Institutional Collaborations

Institution		Topic
CDC, Atlanta, GA, USA		Molecular epidemiology of *V cholerae* 0139
Center for Vaccine Development University of Maryland Baltimore MD, USA		Studies on *V cholerae* and enteropathogenic *E coli*
The Johns Hopkins University USA	1)	Cholera Vaccine evaluation
	2)	Vitamin A
Centers for Disease Control Atlanta USA		Detection of viral diarrhoeal pathogens
University of Virginia USA		Diagnosis of *E histolytica*
University of California Davis USA	1)	Validation of new biochemical methods to assess vitamin A status
University of Alabama Birmingham USA	1)	Investigation of urinary excretion of vit A during acute infection
	2)	Development of methods for vitamin A assessment
Karolinska Institute Stockholm, Sweden		Biochemical fingerprinting of bacterial diarrhoeal pathogens
Karolinska Institute Huddinge Hospital Huddinge, Sweden		Capsule of *V cholerae* 0139
Arrhenius Laboratory, University of Stockholm, Sweden		LPS antigens of enteric bacteria

University of Goteborg Sweden	1)	Immune response to *V cholerae* 0139
	2)	Enterotoxigenic *E coli* Vaccine
University College of Veterinary Medicine Helsinki, Finland		Studies on *Hafnia alvei*
Laboratory of enteric pathogens Central Public Health Laboratory Colindale London, UK		*Shigella*
University of Adelaide Australia		Genetic studies on LPS of *V cholerae* 0139
Armed Forces Institute of Medical Sciences, Bangkok		Studies on *V cholerae*
Naval Medical Research Institute-2, Jakarta, Indonesia		Studies on *V cholerae*
Institute of Microbial Diseases Osaka University, Japan		Studies on *V cholerae*
National Institute of Health Tokyo, Japan		Studies on *V cholerae*
The University of the Ryukus School of Medicine Okinawa Japan		Studies on *V cholerae*
Juntendo University School of Medicine, Tokyo, Japan		Studies on *V cholerae*
Kyoto University School of Medicine, Kyoto, Japan		Studies on *V cholerae*
Institute of Tropical Medicine Nagasaki, Japan		Studies on *V cholerae*
National Institute of cholera and Enteric Diseases,(NICED) Calcutta India		Studies on *V cholerae*
Christian Medical College Hospital, Vellore, India		Studies on *V cholerae*

National Institute of Immunology New Delhi, India	*Shigella* Vaccine development
UAE University, Al Ain, UAE	*Shigella* Vaccine Development
University of Dhaka Bangladesh	Immune response in complicated shigellosis and persistent diarrhoea
Institute of Nutrition & Food Science University of Dhaka	Weaning food
Institute of Public Health Nutrition Dhaka Bangladesh	Weaning food

COMMUNITY HEALTH DIVISION

Institutional Collaborations

Sl	Institution	Topic
01	The Johns Hopkins University, Baltimore, Maryland USA	Micronutrient supplementa-tion, Pneumococcal vaccines, Measles vaccines Epidemiology of diarrhoea and ARI
02	London School of Hygiene & Tropical Medicine, London, UK	Environmental Health Reproductive Tract Infection, Measles Vaccines MCH
03	Centers for Disease Control, Atlanda, USA	Exchange of epidemiological information
04	National Institute for Cholera and Enteric Diseases, Calcutta India	Research on Cholera
05	Dhaka University, Bangladesh	Environmental Health (Research Supervision) Microbiology research supervision Social Sciences
07	National Institute of Preventive and Social Medicine, Dhaka	Teaching and external examinership
08	Independent University, Bangladesh	Teaching
09	Bangladesh University of Engineering and Technology	Teaching and external examiner (M Sc Environmental Engineering)
10	CARE Bangladesh	Hygiene Education/Behaviour change
11	Kumudini Welfare Trust	Epidemniology of diarrhoea and ARI
12	Gana Shahthya Kendra Savar, Dhaka	Health care projects provision and utilisation
13	BRAC	Social and economic developent programme and Health Women development
14	AIDSCAP, Bangkok, Thailand	HIV/AIDS Staff Education
15	Dhaka City Corporation	Water-Sanitation and Environmental studies
16	Government of Bangladesh, National Programme for Control of diarrhoeal diseases	Investigation and intervention of diarrhoeal epidemics in Bangladesh

17	Harvard University ADDR Project	Technical assistance for control of cholera epidemic in Ecuador an Peru
18	USAID	Technical assistance for control of cholera epidemic among the Rwandan Refugees in Goma, Zaire
19	Dhaka Urban Community Health Project	Health care projects, provision and utilisation
20	Radda Barnen (Swedish Save the Children)	Anaemia during pregnancy
21	UNICEF	Water & Sanitation/ applied research in slum improvement a technical assistance Safe motherhood
22	Directorate of Public Health Engineering	do
23	NGO Forum for Water and Sanitation	do
24	5 Local NGOs at district level	do
25	Local Government and Engineering Dept	do
26	Local NGOs in Disaster Management	do
27	Dhaka Shishu Hospital	Neonatal Rotavirus
28	Institute of Post Graduate Medicine and Research, Dhaka Medical College Holy Family Hospital	Pneumococcal Vaccines
29	Dhaka Shishu Hospital	Surveillance serotyping and antibiotic sensitivity of S pneumococci
30	Kantospital Basel, Switzerland	ALRI Research
31	GOB National ALRI Programme	Pilot testing ALRI case management strategy in Bangladesh

POPULATION AND FAMILY PLANNING DIVISION

Institutional Collaborations

Institution	Topic
RAND	Adult health survey
University of Pennsylvania	Family demography
London School of Hygiene and Tropical Medicine	Women s nutritional status and its impact on survival
London School of Hygiene and Tropical Medicine	Improving the Demographic Surveillance System (DSS)
Asian Institute of Technology	Information Technology Strategy
Population Council	Transfer of Matlab lessons to Africa
Population Council	MCH-FP operations research
University of Michigan	Family planning worker studies
Johns Hopkins University	Seasonality of fertility and mortality in Bangladesh
Johns Hopkins University	Urban MCH-FP research
Dhaka University	Measuring levels and trends in vital events
East-West Center	Validating Demographic and Health Survey techniques
Penn State University	Early foetal loss
Georgetown University	Adolescent nutritional status and adult outcomes

CLINICAL SCIENCES DIVISION

Institutional collaborations

Institution	Topic
University of Basle Switzerland	Therapeutic efficacy of oral 5-amino salicylic acid in acute shigellosis
Karolinska Institute, Sweden	Exploratory study of salt and water homeostasis and renal function in children with and without hyponatraemia in association with shigellosis
University of California Davis USA	Assessment of vitamin A status using deuterated retinol dilution technique preliminary study of plasma kinetics in vitamin A depleted and replete adult volunteers
International Atomic Energy Agency Vienna Austria St Mary s Hospital Medical School London UK School of Medicine University of North Carolina at Chapel Hill USA	Vegetable protein source for refeeding malnourished children during recovery from shigellosis
University of Basle Switzerland	Prevalence of *H pylori* infection in rural children of Bangladesh

WHO/CDD

International

- All India Institute of Medical Sciences (India), International Centre for Diarrhoeal Disease Research, Bangladesh (Bangladesh), Instituto de Investigacion Nutricional (Peru), The Aga Khan University and the National Institute of Child Health, Karachi (Pakistan), Hospital Infantil de Mexico Federico Gomez (Mexico) Children's Hospital No 1 (Viet Nam) - Algorithm for the management of persistent diarrhoea in a hospital setting (one conference (Kenya) and 2 workshops - India & Mexico) 1991-1994 (ADDR/WHO)

- All India Institute of Medical Sciences (India) and Instituto de Investigacion Nutricional (Peru) - Algorithm for the management of persistent diarrhoea in a community setting (ADDR & WHO)

- All India Institute of Medical Sciences (India), Instituto de Investigacion Nutricional (Peru), Ministry of Health (Ghana), the London School of Hygiene and Tropical Medicine (UK) and the Johns Hopkins University (USA) - Immunization-linked vitamin A supplementation (multicentre)

- Centre Muraz (Burkina Fasso) and the London School of Hygiene and Tropical Medicine - hygiene research

- Instituto de Investigacion Nutricional (Peru) and the London School of Hygiene and Tropical Medicine - hygiene research

- All India Institute of Medical Sciences (India) and the John Hopkins University - zinc research

- Institute of Child Health Istanbul (Turkey) and the University of Pennsylvania - breastfeeding research

- Universidade Federal da Bahia, Brazil and the London School of Hygiene and Tropical Medicine - Vitamin A research

- ICDDR,B, (Bangladesh), Universidade Federal da Bahia (Brazil) and the London School of Hygiene and Tropical Medicine - research on fluid intake during diarrhoea

- Abu El Reeche Hospital (Egypt) and the Johns Hopkins University - research on low osmolarity ORS

- Instituto de Investigacion Nutricional (Peru) and the University of California Davis - zinc research and complementary feeding research

- Universidade Federal de Bahia (Brazil), All India Institute of Medical Sciences (India), Instituto Nacional de Pediatria (Mexico) and Universidad Peruana Cayetano Heredia (Peru) - multicentre study on low osmolarity ORS

- University of the West Indies (Jamaica) and London School of Hygiene and Tropical Medicine (UK) - research into complementary feeding

- La Leche League (Honduras), University of California, Davis - Breastfeeding research

- Instituto de Investigacion Nutricional (Peru) and Cornell University (USA) - Breastfeeding research

- International Centre for Diarrhoeal Disease Research, Bangladesh (Bangladesh) and Bab El Sha'Reya University Hospital (Egypt) - research into severe diarrhoea

- Instituto de Nutricion de Centro America y Panama, Guatemala and Universidade Federal de Minas Gerias, Brazil - research into use of milk in acute diarrhoea

- Universidade Federal de Pelotas (Brazil), London School of Hygiene and Tropical Medicine, (UK) International Centre for Diarrhoeal Disease Research, Bangladesh (Bangladesh), All India Institute of Medical Science (India), Center for Population Development Studies Harvard University (USA) clinical patterns of diarrhoea mortality

National

- Universidad Peruana Cayetano Heredia (Peru) and the Instituto Nacional del Salud del Nino, (Peru)

- Department of Health, Research Institute of Tropical Medicine University College, La Salle University (Philippines) - Programme impact evaluation

Collaborating Centres

Ten collaborating centres played a role in support of research efforts, in the provision of information and training to other institutions in the areas of epidemiology and vaccine development and evaluation

- WHO Collaborating Centre for Research on Human Rotaviruses
  Department Gastroenterology
  Royal Children's Hospital
  Parkville, Victoria
  Australia

- WHO Collaborating Centre for Research, Training and Control in Diarrhoeal Diseases
  ICDDR B
  Dhaka
  Bangladesh

- Centre Collaborateur de l'OMS pour le Campylobacter entérique
  Hôpital St Pierre
  Bruxelles
  Belgium

- WHO Collaborating Centre for Reference and Research on Escherichia and Klebsiella
  Statens Seruminstitut
  Copenhagen
  Denmark

- Centre collaborateur OMS de Reference et de Recherche pour les Salmonellae
  Institut Pasteur
  Paris
  France

- WHO Collaborating Centre for Diarrhoeal Diseases Research and Training
  National Institute of Cholera and Enteric Diseases
  Calcutta
  India

- WHO Collaborating Centre for Phage-typing and Resistance of Enterobacteria
  Central Public Health Laboratory
  London
  United Kingdom

- WHO Collaborating Centre for Environmental and Epidemiological Aspects of Diarrhoeal Diseases
  Department of Epidemiology and Population Sciences
  London School of Hygiene and Tropical Medicine
  London
  United Kingdom

- WHO Collaborating Centre for Shigella
  Division of Bacterial Diseases
  Centre for Infectious Diseases
  Centers for Disease Control and Prevention
  Atlanta
  USA

Other Agencies and Organizations

The CDD Programme has also collaborated with the following

Academy for Educational Development
Applied Diarrheal Disease Research Project (ADDR)
HEALTHCOM Project (Communication for Child Survival)
International Centre for Diarrhoeal Diseases Research, Bangladesh (ICDDRB)
International Development Research Centre
Swedish Agency for Research Cooperation with Developing Countries
Swedish International Development Authority
Thrasher Research Fund
United Kingdom Overseas Development Administration
UNICEF
USAID Consultative Group on Vaccine Development

Industry

Bayer Diagnostics, France
Dakopatts A/S, Germany
Galactina, Switzerland
Laboratoire Plan SA, Switzerland
Lederle Laboratories, USA
Leo Pharmaceutical Products, Denmark
Pasteur-Merieux, France
Pfizer, Switzerland
Swedish National Bacteriological Laboratory, Sweden
Swiss Serum and Vaccine Institute, Switzerland
Wyeth-Ayerst Laboratories, USA

WHO/ARI

A list of institutional collaboration since 1 January 1991

Pakistan Institute of Medical Sciences (Pakistan), Centers for Disease Control and Prevention (USA) - antimicrobial susceptibility

Ministry of Health (Egypt), Centers for Disease Control and Prevention (USA) - antimicrobial susceptibility

London School of Hygiene and Tropical Medicine (UK), Universidade de Ceara (Brazil) - drug utilization

Pakistan Institute of Medical Sciences (Pakistan), Centers for Disease Control and Prevention (USA) - cotrimoxazole resistance

Centers for Disease Control and Prevention (USA) and Kenya Medical Research Institute (Kenya) - sick child

East West Center (Hawaii, USA) and Institute of Nutrition of Central America and Panama (Guatemala) - Vitamin A, pneumonia morbidity

California Polytechnic State and Institute (USA) of Nutrition of central America and Panama (Guatemala) - indoor air pollution

Department of Economics, Mount Holyoke College (USA) and Centers for Disease Control and Prevention (USA) - Hib vaccines

National Institute of Nutrition (Mexico) and University of Gainesville (Florida, USA) - adapting home care advice

Research Institute for Tropical Medicine and Dr Mary Lung'aho (USA) - local adaptation of messages

Other Agencies and Organizations

Department of Population, Health and Nutrition, World Bank

Child Survival Initiative Unit, Bamako Initiative Unit, UNICEF

BASICS (USA)

Johns Hopkins University (USA)

Liverpool School of Tropical Medicine (UK)

Medical Research Council (Gambia)

Overseas Development Administration (UK)

International Development Research Center (Canada)

Applied Diarrheal Disease Research (USA)

U S Agency for International Development (USA)

Thrasher Foundation (USA)